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# DIABETES.

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# DIABETES:

## ITS VARIOUS FORMS

AND

## DIFFERENT TREATMENTS.

BY

GEORGE HARLEY, M.D., F.R.S.,

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# PREFACE.

This article on the different forms of Diabetes and their various treatments, consists of a part of a course of original lectures on the urine and diseases of the urinary organs which, with slight modifications, I have annually delivered to medical practitioners since the year 1856.

This article was first published in the "Medical Times and Gazette," during last year (1865), and it is on account of its containing much that is novel, both in a practical and theoretical point of view, that I have been induced to reprint it in a separate form.

GEORGE HARLEY.

77, *Harley Street,*
*Cavendish Square, W.*

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# DIABETES MELLITUS.

In no department of experimental research have results of greater value to the clinical physician been recently obtained than in that connected with the study of animal saccharine matter. Within the last few years, indeed (since 1848), an entire revolution has taken place in our ideas of the physiology and pathology of diabetes; and, although we have still much to learn before we can completely unravel the skein of laws regulating the formation and destruction of sugar in the animal economy, we have, nevertheless, reason to congratulate ourselves upon that which has already been achieved, and be sanguine in our expectations of what science may yet accomplish.

Before entering upon the consideration of this important era, which dawned within my own time, and whose gradual development I have not only watched as an interested spectator, but occasionally assisted as a conscientious actor, it will be advisable for me briefly to scan the earlier literature of diabetes, in order that you may better appreciate the advances that have been recently made, and comprehend in what respect the views of its pathology about to be given essentially differ from those of my predecessors and contemporaries.

From time immemorial, cases of emaciation, accompanied by an inordinate thirst and voracious appetite, had been observed, and in consequence of the patients so affected being at the same time troubled with an excessive elimination of urine, ancient physicians gave to the disease the name of Diabetes (δια, through; βαινω, I go). It was not, however, until 1674 that the urine was discovered to possess, in some cases, a sweet taste, the honour of which discovery belongs to an English physician named Thomas Willis. From this time henceforth the disease was divided into two classes, one of which received the name of Diabetes insipidus (without sugar), the other that of Diabetes mellitus (with sugar).

In 1774, exactly one hundred years after the date just alluded to, Mathew Dobson, a physician practising in Liverpool, discovered that the blood as well as the urine in diabetes, contains sugar, and from this observation he justly concluded that the saccharine matter found in the urine is not formed in, but only excreted by, the kidneys.

In 1778 Cowley succeeded in separating the sugar from the urine in a free state. (I may here remark that Bartholdi, so early as 1619, called attention to the presence of saccharine matter in milk; but this is, of course, a point entirely unconnected with diabetes.)

In 1796 John Rollo, surgeon-general to the Royal Artillery, made the first important observation regarding the treatment of diabetes by discovering that an animal diet not only reduces the quantity of urine, but even diminishes the amount of sugar daily eliminated.

The next two steps were made by foreigners.

In 1815 M. Chevreul ascertained that the saccharine matter met with in diabetic urine differs from ordinary cane sugar, and closely resembles that of the grape.

In 1825 another important step was gained by Tiedemann and Gmelin discovering that starch is transformed into sugar during its passage along the alimentary canal.

In 1837 the next observation of interest was made by

M'Gregor, of Glasgow, who found sugar in the vomited matters of diabetic patients—an observation which seemed to confirm Rollo's idea that the disease arises from the gastric juice turning vegetable food into sugar; and from that time till the present animal diet was consequently considered our sheet anchor.

We now arrive at an entirely new phase in the literature of diabetes, in which the teachings of the sick chamber gave place to those of the laboratory.

In 1848 the physiological world seemed as if struck by a thunderbolt when Bernard proclaimed that animals, as well as vegetables, had a sugar-creating power. Until then all the saccharine matter met with in the human body, whether in health or in disease, was supposed to originate in the transformation of vegetable substances. And now, for the first time, were we made alive to the startling fact that men, like sugar-canes, possess within themselves a saccharine manufactory; the liver being daily and hourly as actively engaged in fabricating sugar as in secreting bile.

Like all great discoveries, the rays of this one were not limited to its own field of inquiry, but broadly reflected over the various departments of scientific Medicine. By it new ideas were awakened, new discoveries made, and even at the present hour the impetus it gave to original research is still alike perceptible in the laboratory, in the dead-house, and in the clinical ward. In connection with the subject of diabetes alone, the following may be reckoned as a few of the more important discoveries to which it led:—

In 1849 Bernard discovered that the disease can be artificially communicated to animals by pricking the floor of the fourth cerebral ventricle.

In 1853 I discovered that diabetes may be artificially induced in animals by exciting the liver through means of stimulants, such as alcohol, directly introduced into the portal circulation. An observation which explains the well-known fact that diabetes is a much more common disease in spirit-drinking than other countries.

In 1855 Bernard discovered that the formation of sugar in the liver cannot be regarded in the light of a "vital" process, as it goes on, not only after the death of the animal, but even after the removal of the liver from the body.

In 1856-7 Chauveau and myself gained another piece of ground by ascertaining that the sugar normally present in the circulation is not burned off in the lungs, as hitherto supposed, but disappears from the blood in its transit through the capillaries of the general circulation. The function of the saccharine matter most probably being to nourish the body.

In 1857 Bernard made the additional discovery, that before albuminous substances are converted into sugar, they first pass through the transitional stage of glucogene (animal starch).

Lastly, in 1859-60 Brücke and Jones ascertained, by careful experiment, that traces of sugar are even to be detected in normal urine—an observation which, we shall afterwards see, has an important bearing on the pathology of diabetes; for, as I stated in a previous lecture, it may be regarded as a fundamental law that in disease neither new substances nor new functions are created. Morbid phenomena being merely the result of a change in the quantity and quality of normally existing agents and agencies.

### *Chemistry.*

Although every one knows, or at least imagines he knows, a good deal about the nature and properties of sugar, I shall venture to say a few words upon the subject; for the more extensive our knowledge, the easier will be the comprehension of this hitherto-regarded inexplicable disease. And on the present occasion it is the more necessary for me to do so, seeing that I differ from my predecessors and contemporaries in believing that there are at least two distinct forms of the disease, requiring diametrically opposite lines of treatment—an opinion which I shall presently show is as much in accordance with the teachings of the bedside as of those of the laboratory.

The term "sugar" is applied to a great variety of substances, the common essential character being their sweet taste. Chemists have, however, drawn broad distinctions between the different forms of saccharine matters, the properties of which are exceedingly varied. But for the sake of convenience they have been divided into two great classes—a *first* and a *second*—according to the manner in which they are acted upon by acids, and alkalies.

To the first class, of which *cane sugar* is the type, are given all those that are easily crystallized, and which, when boiled with an alkali, are not decomposed, but enter into combination with it to form a saccharate of the alkali.

To the second class, of which *grape sugar* is the type, are awarded those which are not easily crystallized, and which, when boiled with an alkali, are transformed into the acids of molasses—glucic and melassic acids.

When acted upon by acids, on the other hand, an equally remarkably feature of distinction is observable in these two classes of sugar; for while sugars of the second class remain apparently unaffected, sugars of the first (cane) are rapidly transformed into those of the second class (grape).

These changes are easily illustrated. If, for example, I boil a little sugar candy (a sugar of the first class) with potash, no apparent change is visible; whereas, if before boiling it with potash I heat the solution of sugar candy in a test tube along with a couple of drops of hydrochloric acid, on adding the potash, the whole liquid becomes of a dark brown colour in consequence of the grape sugar (a sugar of the second class) which was formed by the action of the hydrochloric acid upon the cane sugar being instantly decomposed by the potash into the acids of molasses (glucic and melassic).

Just as the vegetable kingdom furnishes us with the two great types of sugar, *cane* and *grape*, so the animal kingdom yields to us their representatives in the form of milk, and liver sugar; milk sugar being the analogue of cane, liver sugar of grape. For example, the sugar of milk is readily crystallized, is unaffected by alkalies, but easily transformed into liver sugar by the action of acids. Liver sugar, on the other hand, is crystallized with difficulty, unaffected by acids, but rapidly decomposed by alkalies.*

Even the relative distribution of the two classes of sugar in the vegetable and animal kingdom is nearly identical; for just as in the vegetable world the sugars of the second greatly preponderate over those of the first class, so in the animal economy, while the second class sugar is to be encountered in the blood, the liver, and the urine, that of the first class is limited to the mammary secretion alone.

*Tests for Saccharine Urine.*—A great variety have been proposed, but I shall only enumerate those possessing a real practical value.

1st. Specific Gravity.—Saccharine urine is generally, though not always, of a high specific gravity, averaging from

* By combining liver sugar with chloride of sodium (common salt), Berthelot and De Luca have succeeded in obtaining large, colourless, transparent crystals, the watery solution of which ferments with yeast, and reduces the oxide of copper. The composition of the crystals, as ascertained by analysis, is represented by the accompanying formula—$2C_{12}H_{12}O_{12},2HO+NaCl$. The authors conclude therefrom that liver sugar is not only exactly the same as that found in diabetic urine, but that it is also identical with the sugar of the grape.—*Compt.-Rend.*, vol. xlix., p. 213.

1020 to 1040. The specific gravity may be much higher, or much lower, even independently of the amount of sugar it contains. For, in diabetic urine there is generally a large excess of urea, which greatly adds to its specific gravity ; and occasionally, on the other hand, the disease is accompanied with an albuminuria sufficient to reduce the specific gravity even to below the normal standard. The specific gravity itself is therefore no criterion of the amount of sugar contained in any given specimen of urine.

2nd. Potash Test.—To a drachm of urine in a test tube add an equal bulk of a solution of potash of the specific gravity of 1060. Heat the upper half of the liquid in the flame of the lamp until it boils ; then mark the change. If sugar be present, the upper boiled portion of the liquid changes colour, and becomes yellow or brown, in proportion to the amount of saccharine matter in the liquid. The browning being due to the transformation of the sugar into glucic and melassic acids. The lower cold half of the liquid, on the other hand, by remaining unaffected serves as a standard of comparison.

3rd. Copper Test.—To a drachm of urine add half a drachm of the potash solution. Shake the mixture, and *afterwards* add a few drops of a solution of sulphate of copper ; * just sufficient to produce a pale blue tint when the whole is agitated. Boil the liquid from the bottom, and if sugar be present the blue colour will disappear, and a yellow or red precipitate form, according to the amount of sugar present in the urine.

The chemical steps of this process are as follows :—When sulphate of copper ($SO_3CuO$) is added to a solution of caustic potash ($KaO$), the sulphuric acid combines with the potash

---

* The most convenient strength I find is ten grains to the ounce of water.

to form a soluble sulphate, and the oxide of copper separates in the form of a gelatinous precipitate, which, however, in consequence of the presence of organic matter, remains suspended in the urine.

$$SO_3CuO + KaO = SO_3KaO + CuO.$$

The next stage in the process is produced by the heat causing the sugar to oxidise itself at the expense of the oxide of copper; whereby the yellow suboxide is thrown down.

$$\text{Sugar} + \left\{\begin{matrix} CuO \\ CuO \end{matrix}\right. = \text{Sugar O} + \left\{\begin{matrix} Cu \\ Cu \end{matrix}\right. O$$

If much sugar be present, and the boiling is continued sufficiently long, all the oxygen is withdrawn from the copper, and the red metal is precipitated on the bottom and sides of the test tube.

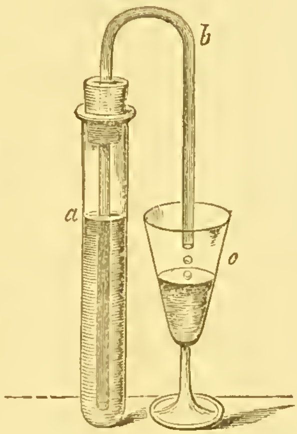
N.B.—Should the urine contain albumen, the albumen must be separated by the aid of heat and acetic acid before applying the copper test. Otherwise, on adding the sulphate of copper to the urine + the potash, a mauve instead of a blue liquid will be obtained; and, on boiling, no reduction of the copper will occur unless a large excess of sugar be present, the liquid merely changing its tint from a mauve to a purple, and from a purple to a red colour.

When the urine contains bile pigment, or is otherwise high coloured, and the sugar is present in small quantity only, it is necessary to decolourise the urine before adding the reagents. For this purpose, put an ounce or two of urine into a six-ounce bottle along with a tablespoonful of animal charcoal and a small pinch of carbonate of soda. Shake the mixture well for a few minutes, and then filter. A perfectly colourless liquid will thus be obtained, and greatly facilitate the application of both the copper and potash tests.

A great deal has been said about the fallacies likely to arise from the presence of uric acid, cotton fibres, chloroform, etc., in the urine. All I can say is, that during a fifteen years' experience, I have never encountered them. In all cases of doubt, however, in addition to the potash and copper, I invariably apply the fermentation test.

4th. Fermentation Test.—The easiest way of applying this to urine is to employ an apparatus like that represented in the accompanying woodcut.

Fig. 24.




A test tube, of about six inches long and three-quarters of an inch in diameter, is to be fitted by means of a piece of cork with a piece of ordinary small glass tubing bent to the shape of a syphon in the flame of the spirit lamp. When ready for use, the tube is filled brimful of urine, to which a few drops of baker's yeast have been added. The syphon is next fixed in the tube by means of the well-fitting cork, and the free end allowed to dip into a glass conveniently placed to receive the liquid as it is driven out of the tube by the carbonic acid generated during the process of fermentation. Each equivalent of sugar is transformed into one of alcohol and four of carbonic acid gas, so that every seventeen cubic centimetres of carbonic acid evolved is equivalent to one grain of sugar decomposed.

During the fermentation process the apparatus must be kept in a moderately warm room.

When diabetic urine is set aside for a few days it frequently ferments spontaneously, and the liquid becomes filled with torulæ, or sugar fungi, which can be readily recognised with the microscope. They consist, like the common yeast plant, of a number of spores strung together in short rows like beads. The sporules of torulæ are, however, smaller than those of yeast, their relative size being represented in Fig. 25. In a few cases I have seen spores of torulæ spontaneously form in urine within twenty-four hours after its emission, although, as a rule, about thirty-six hours are necessary for this development.

FIG. 25.

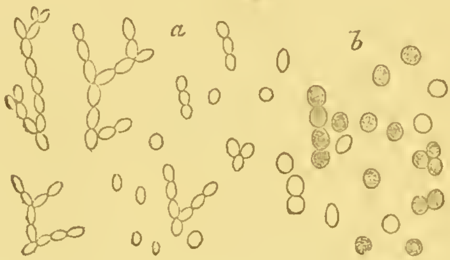



FIG. 25.—*a.* Sporules of Torula Cervisiæ from diabetic urine. *b.* Spores from baker's yeast.

*Quantitative Analysis.*—At one time the quantitative determination of sugar was a long and tedious process, but now by adopting the following method I find it both quick and easy. Three solutions must be retained in readiness :—

1st. A standard solution of sulphate of copper, made by dissolving 34·63 grammes (536·76 grains) of dry sulphate of copper in 1000 c. c. (32·26 oz.) of distilled water. 1 c. c. of this solution represents 0·005 gramme of dry diabetic sugar.

2nd. A solution of caustic potash of the specific gravity of 1060.

3rd. A saturated solution of the bitartrate of potash.

The object of keeping these solutions separate, instead of combining them as is usually done, is in order to avoid the danger of the spontaneous reduction of the oxide of copper, which invariably takes place sooner or later in all the ordinary standard solutions. Having the solutions at hand, place before you two porcelain capsules, each containing an ounce of distilled water; to which add 20 c. c. (measured in glass A, Fig. 8.) of each of the solutions, first adding the copper, then the bitartrate, and lastly, the caustic potash. Next take the measure B, Fig. 4, and pour into it 10 c. c. of urine, and dilute with 90 c. c. of water. The mixture will thus amount to 100 c. c.

The succeeding step is to put one of the capsules over the spirit lamp, and as soon as its contents begin to boil add, drop by drop, the diluted urine, until the blue colour of the liquid entirely disappears. Then place it aside in order that the reduced copper may fall to the bottom, and allow you to judge by the depth of colour of the supernatant liquid if much of the oxide of copper still remains to be precipitated. While this is going on, boil the contents of the second capsule, after adding to it an amount of dilute urine equal to that which was employed iu the first experiment; and should the supernatant liquid in the first capsule turn out to be still blue, add, in addition to the amount already used, 5 c. c. of dilute urine. After boiling for a few minutes, place it aside in order that its reduced copper may fall down, and repeat the same thing with the other capsule until the exact quantity of dilute urine required to reduce the 20 c. c. of standard copper solution be ascertained. So soon as that is accomplished, all that is required in order to find out the quantity of sugar eliminated by the patient in twenty-four hours is to divide the total number of c. c. of urine passed by the number of c. c. of dilute urine required to reduce the 20 c. c. of copper solution.

Suppose, for example, the patient passed, as in case now before me, 3,720 c. c. of urine in twenty-four hours, and 26 c. c. of dilute urine were required to reduce the oxide of copper, the 3,720 divided by 26 would give the number of grammes of sugar contained in the twenty-four hours' urine.

$$3{,}720 \div 26 = 143 \text{ grammes in the 24 hours' urine.}$$

Should the urine contain very little sugar, it is quite unnecessary to dilute it; and in that case, the calculation is made in the usual way, as for example, for urea.

Those who have not the means of making a quantitative analysis in the way above described may adopt the simpler, though less exact, method proposed by Dr. William Roberts. The following is the mode of procedure:—

1. Four ounces of urine are placed in a twelve-ounce phial, with a lump of German yeast of the size of a small walnut.

2. This is loosely corked, or covered with a slip of glass, and placed in a warm place to ferment.

3. A companion phial filled with the same urine—say a three-ounce phial—is tightly corked, and placed beside the fermenting phial.

4. In about twenty-two hours, when fermentation has ceased, the two phials are removed, and placed in some cooler part of the room.

5. Two hours after—that is, about twenty-four hours from the commencement of the experiment—the contents of the phials are separately poured into cylindrical glasses, and the density of each observed.

6. The difference between the two specific gravities is thus ascertained, and every degree of "density lost" indicates one grain of sugar per fluid ounce of the urine.

Crystals of diabetic sugar may be prepared by simply evaporating a few drops of urine to dryness on a glass slide. But this is only possible when the urine is very rich in sugar, and contains but little urea, and other salts. The most characteristic form of crystal is that of of the rhomboidal prism occasionally arranged in arborescent tufts, as represented in the accompanying drawing (Fig. 26), which was kindly made for me by Mr. T. R. Loy, one of the gentlemen attending my practical class. Such crystals are in general called diabetic sugar ; but I believe them to be a combination of sugar and chloride of sodium, for except in the presence of chloride of sodium, diabetic sugar never assumes a so regularly prismatic form of crystallisation. Gibb says that when diabetic urine contains a larger proportion of salts, the sugar crystallises in little circular masses, with minute crystals projecting from the surface. The masses appear to be made up of an aggregation of flat plates of sugar, and, when examined on a dark ground, resemble lumps of the well-known barley-sugar.

Fig. 26.

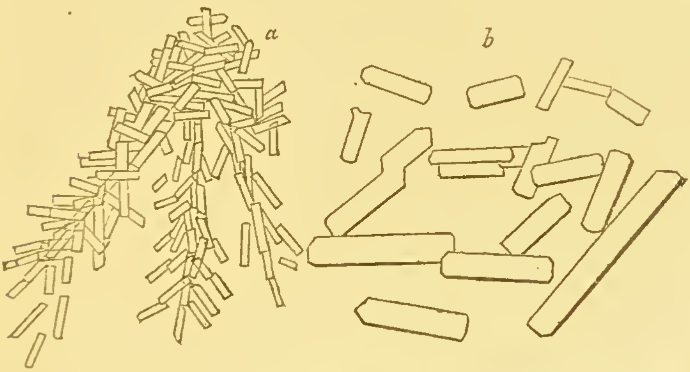



Fig. 26.—Compound crystals of diabetic sugar and common salt, spontaneously formed in concentrated human urine. *a*. As seen under a low power. *b*. Highly magnified.

*Physiology.*

If we desire to be philosophical as well as practical, it is necessary that we should thoroughly understand the origin and destruction of the sugar met with in the animal economy. I shall, therefore, now proceed to the consideration of the *physiology* of diabetes.

That sugar is a normal constituent of the human frame is easily shown by withdrawing an ounce of blood from a healthy man in full digestion, and allowing it to fall drop by drop into a couple of ounces of boiling water faintly acidulated with acetic acid. By so doing all the albuminous matters are so firmly coagulated, that on filtration a perfectly colourless liquid is obtained, and on applying to it the copper, potash, and fermentation tests, the existence of sugar can be demonstrated with facility. Should the patient have had a mixed meal, a great part of the sugar found in his blood will have been directly obtained from the food. This opinion is opposed to the view of Bernard, who on finding that animals have the power of making sugar out of albuminous substances, fell into the error of supposing that all the saccharine matter met with in the human body must of necessity be the product of the liver. The results of my experiments on animals have led me to an entirely opposite conclusion, in as far as the omnivora and herbivora are concerned. This opinion I arrived at from finding abundance af saccharine matter in the blood of the portal vein and chyle of the thoracic duct of a dog, three hours after he had partaken of a quantity of horse-flesh, to which had been added a couple of ounces of soft sugar.

Even in those cases where the patient has had a mixed diet, without, however, having partaken of any sugar in a free state, I still maintain that a great part of the saccharine matter met with in the blood is the direct product of the food, for the following reason :—All vegetable foods, such as bread, turnips, carrots, potatoes, etc., contain a large quantity of starch, which starch during its passage along the alimentary canal is all, or nearly all, converted into sugar through the agency of the digestive juices, especially of the saliva and pancreatic fluids.

The transformation of amylaceous matters into glucose during their sojourn in the alimentary canal is not the result of accident, but the sequence of an unalterable law, which is equally in force in or out of the body, so long as the physical conditions necessary for its action are in operation. Thus, if an ounce of boiled arrowroot, in a test-tube, be mixed with a little saliva, or have added to it half a dozen drops of pancreatic juice, all the starch contained in the arrowroot will infallibly be changed into sugar in the course of a few minutes. And for this operation the intervention of no other agency than that of a temperature equal to that of the human body is required. A precisely similar change occurs in the animal organism, and the sugar thus formed, is absorbed by the mesenteric veins and lacteals, and of necessity forms part of that met with in the circulation.

As regards carnivora, on the other hand, Bernard's assertion is strictly correct, as the result of the following experiment will prove. The experiment was most carefully performed some years ago by Professor Sharpey and myself, with the view of ascertaining not only if sugar exists in the blood of carnivora, but if sugar is actually present in the blood of the healthy animal at the moment of its withdrawal from the circulation.

From the femoral artery of a dog fed solely, during four days, on boiled flesh, perfectly devoid of sugar, one and a half ounces of blood were allowed to flow directly into boiling water, acidulated with acetic acid, and when the clear filtrate from this blood was tested, it gave unmistakable evidence of sugar, which sugar must have been formed in the animal's body, seeing that not a particle of saccharine matter was introduced with the food. It is quite unnecessary for me to cite another experiment in order to prove that the animal organism has a sugar-creating power, for Nature has herself supplied the proofs. Is sugar not a constant ingredient of the normal milk of the flesh-eater, as well as of the vegetable feeder? Most assuredly it is. If the animal body cannot form sugar, from whence does the milk of the carnivora receive its supply? For example, where does the sugar found in the milk of the polar bear come from if it is not manufactured by some organ or other in the animal's own body? Not only does the polar bear live on animal diet, but on the flesh of animals, such as the walrus and seal, whose chief food is fish, which fish, in their turn, are not usually supposed to live upon vegetable matter. As regards this point, I am even inclined to go a step further than Bernard, and not only assert that the carnivorous animal has the power of forming sugar out of albuminous substances, but that even in the case of the herbivorous animal the sugar met with in its milk is not directly obtained from the digestive canal. This, I think, is proven by two facts.

1st. Milk sugar possesses certain special characters which distinguish it from all vegetable sugars.

2nd. Milk sugar, although abundantly present in milk, has not yet been detected in the circulation. The natural conclusion, therefore, is, that it is formed by the mammary gland.

Consequently, it is perfectly clear that there must be at least one organ in the body capable of forming sugar.

Now comes the question—In what organ of the body is the sugar formed which is met with in the general circulation of the carnivora? Answer—The liver. Why the liver? Because, in the case of the carnivora, the blood proceeding to the liver is devoid of sugar, while that coming from it is rich in saccharine matter—richer, indeed, than the blood of any other organ of the body. As Bernard may be considered in the light of an interested party, and I have already cited some of my own experiments, I shall now quote three from an entirely independent observer—Schmidt, of Dorpat;* the results of which are as follows:—

| | Percentage of sugar in Portal vein. | Hepatic vein. |
|---|---|---|
| 1st dog (on animal diet) . . | 0·00 | 0·93 |
| 2nd ,, ,, . . | 0·00 | 0·99 |
| 3rd ,, (fasting during two days) . | 0·00 | 0·51 |

These results I have again and again confirmed, so that there is not the slightest doubt left in my mind regarding their validity, and I believe that they furnish us with the key to the well-known fact that some diabetic patients, even when totally restricted to animal diet, still pass a large quantity of sugar.

Having now ascertained that the healthy blood always contains sugar, and that when the saccharine matter is not obtained from without the body manufactures it for itself, the next point is to determine if sugar be absolutely essential to life, and what use or uses it is put to in the animal organism.

We must begin by finding out if the quantity of sugar in the blood is always the same, or if it be liable to variation; and to what extent.

From the results of a series of experiments made many years ago, I came to the conclusion that the amount of sugar present in the arterial blood of healthy animals is subject to great fluctuations, varying from an almost inappreciable quantity, after long fasting, up to 0·24 per cent. during the time of full digestion. In the hepatic vein the amount, Bernard says, may even be as much as 2 per cent.

The quantity of sugar present in the general circulation

* *Compt. Rend.*, vol. xlix., p. 63.

seems to follow a definite law, for it goes on gradually increasing as digestion advances, and as gradually diminishing as we approach the period for the next meal,—the maximum being reached four or five hours after food, the minimum during fasting. Saccharine matter does not entirely disappear, however, from the circulation till after prolonged fasting. Chauveau found as much as 0·05 per cent. in the blood of a dog, and 0·09 per cent. in that of a horse kept during three entire days without food. In these cases, as the animals were of course forced to live on their own tissues, the sugar formed by their livers must have been made out of some one or other of the constituents of the blood.

The rise and fall in the amount of sugar in the circulation, according to the state of the digestion, is clearly the key to another often-observed pathological fact—namely, that in all cases of diabetes the amount of sugar in the urine is subject to great fluctuations during the course of the day; while it furthermore explains why in some slight cases of diabetes sugar is only to be found in the urine a few hours after a meal.

Having said that the amount of sugar in the blood fluctuates according to the stage of the digestion, it may now be added that the amount of saccharine matter present in the circulation varies in proportion to the quality and quantity of the food. The results of a series of experiments performed in 1858 before the Practical Physiology Class at University College furnish us with the following data:—

In the arterial blood of the carotid artery of three dogs, four hours after having been exclusively fed on horse-flesh, an average of 0·08 per cent. of sugar was found; whereas eight days subsequently, after these same dogs had been freely supplied with mixed diet, consisting of bread, meat, and potatoes, the average amount of sugar in the arterial circulation four hours after feeding rose to 0·22 per cent.,—

hereby affording a physiological explanation of the well-known pathological fact that purely animal diet diminishes, while vegetable or mixed diet increases, the amount of saccharine matter eliminated by the kidneys.

I must now call attention to the fact that, although the quantity of sugar present in the circulation is constantly fluctuating, the amount found in the liver remains comparatively unaltered. Thus, for example, Bernard found, about the same period after death, an average of $1\frac{1}{2}$ per cent. of sugar in the livers of dogs fed exclusively on animal diet, on mixed food, and on vegetable matter,—a result which, from showing that the amount of sugar present in the liver is but slightly influenced by the kind of food, led him into the erroneous idea that diet has no influence on the amount of saccharine matter manufactured by that organ;—a mistake which has constantly brought him into difficulties while attempting to reconcile it with other entirely opposed facts,—such, for example, as the effects of different kinds of foods upon diabetic patients.

The reason why the amount of saccharine matter remains comparatively stationary in the liver while it is constantly fluctuating in the circulation arises from the circumstance of the sugar not being stored up in the hepatic cells, but poured into the vessels as quickly as it is formed; therefore the quantity which the liver at any time contains cannot be accepted as a criterion of the amount which the organ produces. Had Bernard gauged the amount of saccharine matter present in the blood, instead of in the liver, after each particular kind of diet, and drawn his conclusions from the results thereby obtained, he could not possibly have fallen into the above-mentioned error.

Having thus far traced the *rationale* of saccharine urine, we have still to advance a step further, and inquire whether animal food is directly transformed into sugar, or if there is a transition stage in the process between protein substances on the one hand, and saccharine matter on the other. In the case of amylaceous foods, we have already seen there is no connecting link, but that, during their passage along the alimentary canal, they are at once transformed into sugar by certain of the digestive juices. With protein substances, however, the case is very different; for, ere they can be changed into saccharine matter, they must first be resolved into something resembling starch.

I am constantly telling my students that Nature does nothing on a small scale; and the more we study her the more we are forced to admire the uniformity and extensive applicability of her laws. In the vegetable and animal kingdoms we not only encounter analogous substances, but we find that they are endowed with similar properties, and respectively perform similar functions. We already saw that, while the sugar of the cane has its analogue in that of the milk, the sugar of the grape has its analogue in that of the liver. I have now to point out how even vegetable starch has also its analogue in the animal world.

Although the discovery of a substance in the animal body possessing the properties of starch had been long suspected, it was not until 1857 that a large enough quantity was separated in a sufficiently pure state to admit of its being subjected to elementary analysis, and thereby allow its striking affinities to vegetable starch to be demonstrated. To Bernard belongs the credit of having first obtained this substance from the liver in a free state, and shown its direct convertibility into saccharine matter, in consequence of which he appropriately gave to it the title of glucogene.

Glucogene has such a striking resemblance to vegetable starch that a short description of its appearance and properties will not be out of place. Like ordinary starch, it is a neutral, white, odourless, insipid substance; soluble in water, but insoluble in alcohol and acetic acid. When boiled with diluted mineral acids, or treated with either saliva or pancreatic juice, it is transformed, like other amyloid substances, into sugar of the second class. That is to say, into a sugar possessing the property of reducing the oxide of copper, and of being decomposed by caustic potash into glucic and melassic acids. Moreover, it is also, like starch, transformed by fuming nitric acid into xyloidine, a combustible substance, which detonates with flame when heated to 180°.—Poggiale.* On the other hand, it differs from ordinary starch in giving with the tincture of iodine a reddish violet, instead of a deep blue colour. In which respect, therefore, it appears to stand between starch and dextrine.

The easiest mode of extracting glucogene from the liver is to add to a concentrated aqueous decoction of the hepatic substance an excess of glacial acetic acid, which instantly precipitates all the glucogene, and leaves the albumen in solution. The precipitate is then separated by filtration, redissolved in water, and again precipitated by absolute alcohol; the process being repeated until the substance separates in a perfectly pure state.

While giving credit to Bernard for being the first to extract glucogene from the liver, I must not omit to yield to Hensen his proper meed of praise in having foreshadowed the discovery by his researches on the saccharine function of the liver published in 1856,† in which he stated that he had found in the liver of rabbits a yellow substance transformable into sugar by the action of saliva, pancreatic juice, and even portal blood.

According to Pelouze, glucogene is composed in 100 parts of

* Brown-Séquard's *Journal*, 1858, p. 549.

† *Verh. Med. Phy. Gesell.*, Würzburg, vol. vii., part 11, 1856.

| | |
|---|---|
| Oxygen . . . . | 54·1 |
| Carbon . . . . | 39·8 |
| Hydrogen . . . . | 6·1 |
| | 100·0 |

Glucogene has been detected in the livers of all animals in which it has hitherto been sought for, no matter whether they were animal or vegetable feeders, and consequently the natural conclusion is, that the liver possesses the power of forming it out of animal as well as vegetable food. But while, in the case of carnivora, glucogene is only met with in the liver, in that of the herbivora it has been encountered in various other situations: for example, Poiseuille and Lefort found in the blood of a bull 0·073 per cent. In the chyle 0·123 per cent., and in the lymph 0·266 per cent.* It is even to be met with in the muscles. Here is a beautifully pure specimen of glucogene, given to me by Professor Scherer, which he obtained from the muscles of the horse. Moreover, the quantity of glucogene in the livers of herbivora is many times greater than that met with in those of the carnivora.

Now comes the question, What are the uses of glucogene in the animal economy?

We all know that starch, as starch, cannot nourish the body, and from certain facts presently to be related it is highly probable that glucogene must, like ordinary starch, be transformed into saccharine matter, before it can play its part in the intricate processes of life. We already know that at least a great part of the glucogene formed in the liver is changed into sugar before it is permitted to leave that organ. We are also acquainted with another exceedingly interesting and important fact, namely, that, be the transforming agency what it may, it is quite independent of any

* *Comptes-Rendus*, April 5, 1858, p. 645.

so-called vital influences. The transformation of glucogene into sugar appears to follow the same unalterable law as that already noticed regarding the transformation of ordinary starch, for not only does it continue in force after the death of the animal, but even after the removal of the liver from the body. All that is required apparently being the sustaining the organ at a certain temperature.

This assertion can be easily proved by taking the liver of a healthy animal, and after it has been, as far as possible, completely freed from sugar by passing a current of water through its vessels, keeping it in a warm apartment for six or eight hours. The tissues of the organ will then be found saturated with sugar, although only a small quantity could be detected immediately after its removal from the body.

The results of the following experiment,* which was performed by Professor Sharpey and myself, will give a tolerable idea of the rapidity with which glucogene is transformed into sugar in a liver after its removal from the body :—

A dog which had been previously fed on animal diet received a full meal of bread and milk. Five hours afterwards the animal was pithed, and a portion of the liver rapidly sliced off and immersed in a freezing mixture. The portion of frozen liver was found to contain only 0·333 per cent. of saccharine matter; whereas another portion of the same liver, which had not been frozen, after having stood two hours, was found to contain 1·55 per cent.—that is to say, nearly fivefold more of sugar, which sugar had, of course, formed at the expense of the glucogene after the death of the animal. The 0·333 per cent. represents, of course, the amount of sugar present in the liver at the moment of death—an amount which appears insignificant until it is recollected that during life the sugar formed in

* *Proceedings* of the Royal Society, No. 38, p. 289. *Lancet*, October 20, 1860, p. 386.

the liver is removed from it with every pulsation of the heart; consequently, the quantity poured into the circulation during the twenty-four hours must be very considerable, notwithstanding that during life only a fractional part of a per cent. is present in the organ at any one time.

I may here mention that it is this circumstance now alluded to, of there being but a very small quantity of sugar in the hepatic organ at the moment of death, while a large amount is to be found some hours afterwards, which has led Dr. Pavy into the error of supposing that the formation of sugar in the liver is in all cases due to a post-, instead of an ante-mortem cause. Were we to adopt such a mode of reasoning, we might, with equal justice, say that no starch is changed into sugar in the digestive canal during life; for as its transformation likewise still continues after death, the longer we delay in making the analysis the greater is the amount of sugar there found. In fact, under certain circumstances, the duodenum of an animal, immediately after death, may contain only a trace of sugar, and yet an enormous amount be found in it in about half an hour later. The reason of this being, that so long as the animal lived the sugar was absorbed from the intestine by the veins and lacteals, as rapidly as it was formed. Whereas, although when it died the absorption process became arrested, the transformation of the starch into sugar by the pancreatic juice still went on. I need not take up any more time by discussing this question here; but refer those specially interested in the subject to the published writings of Thudichum,* Beale,† and myself.‡ I may only further remark that, even supposing that *not a trace of sugar* could be detected in the liver immediately after death, it would be no more scientific evidence

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* *Brit. Med. Jour.*, March 17, 1860.

† "Urine and Calculi." Second edition, p. 236.

‡ *Proc. Roy. Soc.* No. 38, p. 289.

that the liver did not manufacture sugar during life, than the finding no urine in the kidneys after death would be that the normal function of these organs was not to eliminate urine. A few more substantial data than any hitherto brought forward are required, ere we can venture to accept of negative results in the place of positive facts.

The next point is, "What becomes of all the saccharine matter?" Bernard thought that it was burned off in the lungs, its chief office being to sustain the animal heat; but, as Chauveau and I pointed out, such a doctrine is utterly untenable, seeing that when the experiments are properly performed there is almost as much sugar to be found in the blood returning from the lungs as in that going to them. Thus, for example, in a fasting animal I found that while the blood of right side of the heart contained 0·10 per cent. of saccharine matter, that of the left contained very little less—namely, 0·085 per cent.* In another experiment, performed upon a cat, the blood of the right side of the heart contained 0·18 per cent. of sugar, and that from the left an exactly similar amount; and in order to be certain that no mistake had been made in the determination of the sugar by the volumetric process, I carefully collected the reduced oxide of copper, dried, and weighed it. The amount of precipitate from both bloods was identical.

When one takes into consideration the nature of the lungs, he cannot be surprised at these results; for the lungs are not laboratories, like the stomach, but merely an aggregation of little sacs whose function is purely physical —at least, in so far as respiration is concerned. The only "vital" offices they perform are simply those required for their own development and preservation. The absorption of oxygen and exhalation of carbonic acid would perhaps

* For the manner in which the experiments were performed, see the author's paper in the *British and Foreign Quarterly Review*, July, 1857, p. 201.

go on just in the same way if a piece of goldbeater's skin supplied the place of the air vesicles; for the blood arriving there for the purpose of arterialisation never leaves the capillaries to become in any way incorporated with their tissue.

Does the saccharine matter disappear, then, in the capillaries of the general circulation? It would appear so, for both Chauveau and myself have proved, by carefully executed experiments, that less sugar is to be found in the veins returning from a limb than exists in the arteries going to it. Thus, in the blood from the femoral artery of a middle-sized dog in full digestion I found 0·24 per cent., while that of the corresponding vein contained only 0·16 per cent. of saccharine matter. From its thus disappearing in the capillaries, one is naturally led to believe that it plays a part in the nutritive process. We know, indeed, that while bees have the power of transforming sugar into wax, man and other animals change it into adipose tissue. The negroes are said to become fat and lazy during the sugar harvest from sucking the fresh canes, and long before the days of Bantingism all medical men were aware that babies fatten on sugar quicker than anything else. In 1856, while investigating the uses of sugar in the animal economy, I gave cats and dogs large quantities of sugar-candy along with their other food, and I invariably found that, although they all seemed to like the mixture, and became fat and sleek upon it, a period at length arrived when they notably ceased not only to gain weight, but also to relish the food. In fact, at length some of them would rather starve than touch meat mixed with sugar. It must be remembered, however, that I was giving them enormous doses—from two ounces to a quarter of a pound daily. When the sugar was given in moderation no such effects were observed.

The last point connected with the physiology of the glucogenic function which it is essential for us, as Practitioners, to understand, is the origin of the nerve-force which calls it into play. Bernard has shown that, by dividing the pneumogastric nerves in the neck, the secretion of sugar is at once arrested, and that the application of galvanism to the upper ends of the divided nerves not only re-establishes the secretion, but, if the current be continued sufficiently long, augments it beyond the normal amount, so that animals thus operated upon not unfrequently become diabetic. On the other hand, the application of galvanism to the lower ends of the divided nerves is not found to be followed by any such result. These experiments clearly indicate that the nerve-force which excites the liver to secrete saccharine matter does not travel from the brain, through the pneumogastric nerves to the liver, but rather that the stimulus proceeds along these nerves to the brain, and is from thence re-transmitted to the hepatic organ through some other nerve-chain.

The data yielded by other experiments, which it is at present unnecessary to recapitulate, induced Bernard to believe that in the healthy animal the reflex action which incites the glucogenic function originates in the stimulus given by the respired air to the pulmonary branches of the pneumogastric nerves, and that this stimulus is reflected from the brain along the spinal cord and splanchnic nerves to the liver.

The point of departure of the normal nerve-force which calls into play the glucogenic function of the liver may, at the first glance, appear a matter of little moment; but when we consider that the secretions of organs increase in proportion to the amount of stimulus applied to their nerves, and that an excess of secretion, which not unfrequently constitutes disease, arises in many cases simply from an exaggeration of the normal stimulus, we shall at once acknowledge the importance of thoroughly understanding the physiological, before attempting to remedy the pathological condition of an organ. When an answer has been given to the query, "Where is the sugar secreted?" the question next in importance to the Physician is most assuredly, "By what means is the secretion excited?" A satisfactory answer to the latter question may not improbably furnish a guide to the successful treatment of a hitherto considered incomprehensible disease.

There is no difficulty in accounting for the liver being excited to secrete sugar when an irritation is applied to the pulmonary branches of the pneumogastric nerve; but we are not necessarily forced to believe that they are the branches which normally call into action this peculiar function of the organ referred to. Indeed, if such be in reality the case, how does it happen that while the respiration, and consequently the stimulus, continue at about the same rate during the entire day, the secretion, which is said to be the result of the stimulus, varies at different times? At one hour it is known to be exceedingly active; at another, somewhat later, almost dormant. Such a result has no parallel in any other organ of the body. A certain amount of stimulus, *cæteris paribus*, invariably calls forth a similar and definite amount of action; and upon what grounds are we warranted in considering the function of the liver an exception to the general rule? I need scarcely detain you at present with further arguments against what appears to me an untenable hypothesis, as I believe the results of the subjoined experiments clearly indicate, that *if* the pneumogastric is the nerve which carries the stimulus to the brain, to be from thence transmitted by the spinal cord and splanchnic nerves to the liver, the point of departure of the stimulus is most probably in the liver itself, and that the cause of the reflex action may originate in the stimulating effect of the portal blood upon the hepatic branches of the pneumogastric nerve. If, for example, the stimulating effect of the blood of the portal vein be imitated as much as possible by injecting into that vessel substances, such as alcohol, ether, chloroform, methylated spirit, or ammonia, the liver is excited to secrete an excess of sugar, and the animal operated upon is for a time rendered diabetic.*

The conclusion to which the results of the experiments led me was, that stimulants produce diabetes by exciting the hepatic branches of the pneumogastric to transmit an impression to the nervous centre, to be from these reflected to the liver, and thereby cause the increased secretion of saccharine matter ; and if this explanation be the correct one, it is very probable that the normal secretion of sugar is caused by the stimulating effect of the nutritive materials in the portal blood. The following facts materially strengthen this view:—During the time of digestion the blood of the vena portæ must, of necessity, prove most stimulating, as it is then loaded with nutritive materials ; and this happens to be exactly the period at which the greatest quantity of sugar is formed. On the other hand, the blood of the portal vein of a fasting animal contains very little nutritive material ; consequently during this period the quantity of sugar ought to be lessened, and this, in fact, is exactly what occurs ; for, in a fasting animal, the secretion of sugar has invariably been found to be at its minimum.

The important bearing of these physiological data will be more fully appreciated when we are considering the pathology of diabetes ; for, as will be presently seen, they furnish us with a key to the rational treatment of some of the forms of saccharine urine.

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* For a full account of these researches, see an article by the author in the *Brit. and Foreign Quarterly Rev.*, July, 1857.

### *Pathology.*

We now come to what, at least as far as we, as practical Physicians are concerned, may be considered the most important part of our subject,—namely, its pathology. Diabetes happening, however, to be one of those intricate diseases leaving behind it no characteristic anatomical lesion by which a clue to its seat can be obtained, it is not in the dead house, but in the clinical ward and physiological laboratory that the nature and treatment of the affection are most successfully studied. What has now to be said of its pathology and treatment will, therefore, be found greatly simplified by the knowledge we have already obtained of its physiology. In fact, we shall soon find that the presence of sugar in the urine, like the discoloration of the skin in jaundice, is not of itself the disease, but merely the most prominent sign of several widely-differing abnormal conditions, the correct appreciation and understanding of which entirely depend on our acquaintance with its physiology.

Diabetes has, for example, been found to follow upon—

Injury to the head, with or without fracture of skull.

Clot in the pons varolii.

Softening of the base of the brain.

Abscess of the cerebellum extending into the fourth ventricle.

Tumour (the size of a nut) in the left lobe of the cerebellum.

Disease of the sympathetic nerve.

Tumour of the pneumogastric nerve.

Deposit of bony spiculæ in the falx.

Excessive brain work.

Intense grief.

Sudden mental shock.

Blow on the epigastrium.

Pregnancy.

Uterine disease.

Disordered digestion.

Exposure to cold, etc.

Even in some instances diabetes seems traceable to hereditary constitutional peculiarity, for not only is it occasionally met with in more than one member of the same family, but it has even been found present in parent and child to the third generation. Thus we find it related * that Dr. Mosler had a patient whose father, mother, and two sisters died of diabetes, and that within three weeks after the woman came to the Hospital, her son, aged 15, also presented himself, suffering from the same disease.

Seeing, then, that diabetes springs from a multitude of causes, and that the symptom of saccharine urine is not itself the disease, but merely the most prominent sign of the hidden complaint, we can easily understand how a variety of morbid actions, quite distinct from each other, and perhaps of a diametrically opposite character, may produce it. For example, if the normal stimulus of the liver be exaggerated, an abnormal amount of sugar will be secreted; and if the quantity formed be greater than the amount requisite to supply the wants of the system, the excess, which then acts towards the organism as a foreign body, will be eliminated along with the urine, and the disease diabetes mellitus established. On the other hand, the case may be reversed, and there may still exist an abnormal amount of sugar in the blood to be eliminated with the urine, notwithstanding that only the proper amount has been secreted by the liver. This, of course, must of necessity happen when from any

* *Brit. Med. Journ.*, Dec. 31, 1864.

cause the process of assimilation has been interfered with, and the body fails to consume its normal quantum of saccharine material.

Hence, it is evident that we may have two perfectly distinct forms of the same disease, one of which might be named *Diabetes from excessive formation;* the other, *Diabetes from defective assimilation* (mal-nutrition).

I shall presently have occasion to show that this theory is equally supported by clinical observation as by the results of scientific inquiry. It will be found, too, that it furnishes us with a logical explanation to the fact which is so familiar to all who have had much experience with diabetic cases—namely, that while one man improves and gains both weight and strength on animal diet, another on the same regimen loses both flesh and energy, notwithstanding a diminution, perhaps, taking place in the amount of sugar excreted.

Piorry's idea of curing diabetes by giving, instead of withholding, saccharine matter, may after all turn out to have more reason in it than at first sight appears. Like the animal diet system, however, it will be found only applicable to a certain class of cases. The great point for us, then, is to be able to discriminate between the two forms of morbid action, in order that our plan of treatment may be the one best adapted for the particular case.

How can this be done? Fortunately, the two forms of diabetes have certain peculiarities connected with their history which enables us in most cases to distinguish the one from the other.

In those resulting from *excessive formation* the patient is not necessarily emaciated and weak. He may, on the contrary, look both fat and ruddy—appearing, in fact, to be in the very bloom of health. This is especially true in slight cases, as well as in the early stage of even those which run on to a fatal termination. In this class of patients it is not until the disease has made considerable inroads on the constitution that there is any marked emaciation.

In the second class of cases, on the other hand, namely, those resulting from *defective assimilation*, emaciation is one of the earliest and most prominent symptoms, the loss of flesh being often very marked before the nature of the disease is detected. Exactly the reverse of what frequently occurs in the first class, in which the patient occasionally receives the first warning of the affection from the accidental detection of sugar in his urine.

An inordinate thirst and excessive elimination of urine is in all cases an indication that the disease is already in its second stage, the first stage being indicated, in those arising from *excessive formation*, by saccharine urine alone, and in those from *defective assimilation* by saccharine urine coupled with loss of flesh.

At one time, when a patient was said to have diabetes, it was considered tantamount to saying his days were numbered. As our knowledge has increased, however, we have learned that although it is but seldom possible for us to eradicate the disease, we can, nevertheless, so mitigate its effects as not only to prolong the life of the individual, but to render it a tolerable, if not even an agreeable one. Prout used to declare that diabetic patients are for ever standing on the brink of a precipice, for they are in constant danger of succumbing from the indirect as well as the direct effects of the disease, in consequence of there being in them an absence of that vital stamina which enables healthy persons to resist the inroads of disease. This is, no doubt, true, for the mal-nutrition which diabetes induces renders the constitution prone to take on low inflammatory actions, which, if set up in a healthy individual, would produce but a temporary illness, but when engendered in the diabetic, rapidly run on to a fatal termination. But, as forewarned is forearmed, this need not distress, but only make us the more careful at once to remedy any trifling deviations from the normal standard, which, in the healthy, might be allowed to pass unheeded.

Having only specified two forms of diabetes—1st, That by *excessive formation;* 2ndly, That by *diminished assimilation* —it may naturally be asked how this statement can be reconciled with the one previously made regarding the multitude of causes inducing the disease? Easily enough, as we shall now see.

*Nerve Lesion and Disease as a Cause of Diabetes.*

It is generally admitted that the various secreting organs of the animal body are stimulated to perform their different functions by direct and reflex nerve action, and the liver proves to be no exception to this law. If the pneumogastric nerves be divided in the neck, the glucogenic function of the hepatic organ is arrested, and when galvanism is applied to the upper (but not to the lower) ends of the divided nerves the saccharine secretion is re-established. Moreover, it has been ascertained that this reflex nerve-force, which travels by the pneumogastric nerves to the brain, is from thence reflected along the spinal cord, splanchnic nerves, and solar plexus, to the liver. (Bernard.) It has been further ascertained that it is not at all essential that the galvanism be applied to the cervical portion of the pneumogastric in order to re-excite the saccharine secretion, for, according to another well-known physiological law, irritation produced at any point of a reflex nerve circuit is invariably followed by the same phenomena.

As what I am now attempting to explain is the keystone to the comprehension of the pathology of diabetes by nerve influence, it is absolutely essential that my meaning should be clearly understood. I must, therefore, solicit your attention for a moment to the following experiment:—

Let the hind legs of a frog be prepared in the manner represented in the accompanying woodcut, every attachment being severed except that of the sciatic nerves with the spinal cord. Besides this, let the motor roots be divided on the right side (Fig. 27, *a-b*), and the sensory roots on the left (*c-d*), so as to leave only one complete nerve-chain. The application of a slight galvanic current to the toes of the


FIG. 27.—Reflex circuit in hind legs of frog attached to the spinal cord *a-b*, anterior motor roof of (*g*) right sciatic nerve. *c-d*, posterior sensory root of (*h*) left sciatic nerve.

right limb will then be instantly followed by contractions in the muscles of the left, showing that the nerve stimulus is transported through the sensory nerve of the right limb to the spinal cord, and reflected from thence, through the motor nerve, to the muscles of the left extremity. In order to produce this muscular movement, however, it is not at all necessary that the galvanism be applied at the extremity of the sensory nerve; for irritation produced in any part of its course (*g*, for example), at its root (*e*), or even in the opposite nerve chain (*h*), will still be followed by the same muscular contractions. Now, it so happens, with regard to the glucogenic function of the liver, that the pneumogastric is the analogue of the sensory, and the spinal cord and splanchnic of the motory nerves of the frog's limb ; so that an irritation applied to any part of the pneumogastric nerves, spinal cord, or sympathetic reflex glucogenic circuit, is as effectually followed by a secretion of sugar as the application of galvanism to the sciatic nerves of the frog's limb is followed by muscular contraction. Moreover, the irritation, galvanic or other, has only to be applied to the glucogenic circuit sufficiently long or sufficiently powerfully in order to induce saccharine urine. Hence it is within the power of the physiologist to render animals artificially diabetic by a variety of experimental procedures implicating the various parts included in the reflex nerve-chain above indicated. Thus diabetes can be artificially established by applying the irritation to the extremities of the pneumogastric in the liver; as when stimulants are injected into the portal vein (the author), or by irritating the pulmonary branches distributed in the lungs, as where chloroform is inhaled (Reynoso), or by applying galvanism to the cervical portion of the nerves, or by irritating their roots, as when injury is applied to the floor of the fourth ventricle (Bernard), or by acting on the downward chain, as, for example, when the splanchnics are divided (Graffe). In fact, I might go on to prove experimentally, that the *rationale* of saccharine urine, by reflex nerve action, is as comprehensible as the *rationale* of the muscular contraction in the frog's limb. Nay more, just as we may have muscular contraction following upon the *indirect* application of a stimulus to the nerve in the frog's limb ; so we may have saccharine urine following upon the indirect application of the stimulus to the glucogenic circuit.

For example, diabetes may be induced by a blow on the epigastrium, or from an injury to the head, as in the case which I already cited in a previous lecture. The patient at the time he was admitted into University College Hospital under the care of my colleague, Professor Erichsen, was suffering from paralysis consequent upon injury to the head received in falling from a scaffold. It may be mentioned that it was in consequence of the man having fallen upon the occipital region, that I suggested the possibility of his being diabetic, and had the urine tested. In this case sugar was found the very first time the urine was examined, so that it is impossible to say when it first became saccharine; no sooner was the sugar detected, however, than the nurse was ordered to collect daily all the urine voided during the twenty-four hours, and transmit it to the laboratory for quantitative analysis.

The analyses were made by my former pupil, Dr. Pringle, and the following is a table of the results:—

| | Quantity of urine. | | | Quantity of sugar. | | |
|---|---|---|---|---|---|---|
| 1857. | In cub. centim. | | Oz. | Grammes. | | Grains. |
| July 18th . . | 952 | = | 30·7 | 2·38 | = | 36·89 |
| 20th . . | 1000 | = | 32·2 | 5·00 | = | 77·50 |
| 21st . . | 2187 | = | 70·5 | 6·38 | = | 98·89 |
| 22nd . . | 1875 | = | 60·5 | 3·90 | = | 60·45 |
| 25th . . | 1955 | = | 63·6 | 3·48 | = | 53·94 |
| 28th . . | 1000 | = | 32·2 | 1·25 | = | 19·37 |
| 31st . | Not sufficient sugar for quantitative analysis. | | | | | |
| Aug. 3rd . | No sugar. | | | | | |

It will be seen that at first, after the receipt of the injury, the sugar went on steadily increasing, and then, as the patient recovered, it as gradually steadily diminished, until at length it entirely disappeared.

This was prognosed when I first saw the case. For the condition of the man, as far as his diabetes was concerned, was exactly similar to the state of rabbits rendered artificially diabetic by puncture of the fourth ventricle, and we all know that at first the amount of sugar gradually augments until the injury in the cerebral substance begins to heal, and then the diabetes as gradually disappears.

Some may say, we had no proof beyond the existence of saccharine urine that injury had occurred to, or in the neighbourhood of the fourth ventricle. This is very true, but I think the reasoning from analogy justifies the diagnosis. However, as some may be sceptical on this point, I shall now cite a case where the diagnosis may be said to have been verified by the post-mortem examination.

On November 13, 1859, a man was brought to University College Hospital in a state of insensibility, with slow, stertorous respiration, a weak pulse, and contracted pupils. As the patient died without ever regaining consciousness, the only history of the case that could be obtained was, that he was seen suddenly to fall down in the street, and when picked up was in a state of complete insensibility. At the autopsy, the only lesion found was a clot encircling the medulla oblongata and extending upwards into the pons Varolii, its situation being apparently such as to have caused considerable pressure on the fourth ventricle and roots of the pneumogastric nerves. The presence of sugar in the urine was sought for, and in this case was demonstrated without the least difficulty. Although no quantitative analysis was made, there can be no doubt that the sugar was abundant, as the urine became quite brown on being boiled with potash, and freely reduced the oxide of copper. The flow of urine must have been also copious, as the bladder was found greatly distended by it after death. The substance of the liver contained a large amount of sugar, and even the brain itself was impregnated with the saccharine matter, for an aqueous decoction yielded all the reactions in a very decided manner. Now, unless we are to suppose that this patient had been previously suffering from diabetes, of which his body presented none of the external signs, one is led to the conclusion that the saccharine urine was the direct result of the pressure of the clot on the fourth ventricle.

Another case of diabetes from external injury to the head may be mentioned, as it, like the one already cited, affords an example of spontaneous cure. The urine of a woman, under the care of Dr. Todd, who had hemiplegia and rigidity of the right side, in consequence of falling down stairs upon her head, when examined on the twentieth day after the injury was found to be of a specific gravity of 1021, and to contain a small quantity of sugar, which gradually disappeared as the patient got well.

Several years ago, Dr. Goolden had a case of a similar kind in a railway stoker who was struck on the occiput by the handle of a crane, and remained diabetic during his illness.* Some nerve lesions give rise to a diabetes of a still more permanent character, as the following case will show. Dr. Ramsbotham, of Amwell Street, informs me that when on a visit to a medical friend in Kent, a year or two ago, he found him in a fair state of health, with the exception of feeling extreme thirst, and suffering from great languor. Suspecting diabetes, he examined the urine, and found it to be above the average in quantity, of a specific gravity of 1044, and loaded with sugar. The gentleman had never suspected that he was diabetic; it is therefore impossible to say how long this state of matters had existed. The important part in the history of the case is, that four or five years previously he had been thrown from a horse, and in some way or other got his head forcibly bent forwards, and for a length of time afterwards he could not turn it to either side without great pain; at the same time both the senses of smelling and hearing were blunted. The last report Dr. Ramsbotham had of the case was that "the diabetic

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* *Medical Times and Gazette*, May 15, 1858.

symptoms were ameliorated, or, at any rate, had ceased to be a source of annoyance."

While calling attention to these cases of diabetes, the result of cerebral lesion and disease, I must not omit to mention that an inordinate flow of urine may follow upon concussion of the brain without being associated with the presence of sugar. An interesting case of this kind was observed in M. Moutard, Martin's wards, in which, after a concussion of the brain, followed by hemiplegia, the patient suffered from extraordinary polydipsia. Under the influence of a seton, the cerebral symptoms amended and the polydipsia entirely disappeared.*

As cases of polydipsia are not common, and some authors have even entirely doubted their existence, I may mention an interesting case related by Dr. Watson :—A boy, aged 11 years, who was very thin, but not unhealthy looking, was troubled with thirst and frequent micturition, passing daily nine or ten pints (180 to 200 ounces) of pale dilute urine, of a specific gravity of 1002—sometimes, indeed, scarcely heavier than distilled water. Every remedy was tried, but he left the hospital no better than when he entered it. Even when his drink was limited to a pint and a half, he still passed ten and a half pints of urine.†

In a case of my own, a man, aged 57, passed, on an average, eight pints (4960 c.c.) of urine of a specific gravity of 1010 in twenty-four hours, the daily average of urea being 70 grammes (1085 grains). Notwithstanding that the patient passed so much urine, he only drank about half that quantity of liquid, and, strange to say, although he had an exceedingly dry skin, he never complained of thirst. The polydipsia had lasted three years, and during that time he lost forty-two pounds in weight. No sugar was ever detected in his urine.

Cerebral disease—not consequent on injury—may also be

* *Gazette des Hop.*, No. 18.

† Lect. on the Practice of Physic, vol. ii., p. 611.

productive of saccharine urine. Thus, for example, epilepsy is occasionally accompanied by diabetes.

In a case of this kind which occurred in the Hospital for the Epileptic and Paralytic, under the care of Dr. Brown-Séquard, the pons Varolii and calamus scriptorius of the fourth ventricle was found diseased.* The man, aged 53, whose urine was of a specific gravity of 1037, and "contained a good deal of sugar," had increased sexual desire before death.

A short time since I examined the urine in a case of Dr. Hughlings Jackson's, in which, with disease in the near neighbourhood of the apex of the calamus scriptorius, there was for several months sugar in the urine.

M. Luys related to the Paris Anatomical Society a case of diabetes which lasted over three or four years. At the autopsy the anterior wall of the fourth ventricle was found highly vascular and its consistence notably diminished, very slight scraping bringing off a gelatinous pulp of a brownish yellow colour, the ventricle exhibited the colour very remarkably at certain spots. The lesion consisted in the molecular destruction of the histological elements, and their *débris*, loaded with yellowish granulations, gave rise to this peculiar colour. This lesion may be regarded as exactly corresponding to the traumatic one produced by the experimental physiologist which leads to an exaggeration of the glucogenic function of the liver and the consequent passage of sugar into the urine.†

In other cases of cerebral diseases diabetes also occurs. Thus, Laudet ‡ mentions the following four cases in which he observed it. The first is that of a woman, aged 32, who while pregnant was affected with the loss of vision of the left eye, without paralysis. She at the same time suffered from

* Lockhart Clarke in Beale's *Archiv.*, vol. iv. p. 147.

† *Bulletin* de la Soc. Anatom., vol. v., p. 219.

‡ Acad. des Sciences, March 2, 1857.

vomiting and headaches, and on one occasion had symptoms of coma accompanied by paralysis of the third and fifth part of cerebral nerves. These symptoms were accompanied with great thirst and the other signs of diabetes mellitus. Under the administration of iodide of potassium the paralysis and diabetes diminished.

The second was that of a woman, aged 53, suffering from hemiplegia and epilepsy, supposed to have originated in apoplexy. Two years later diabetes appeared, and in one year more also albuminuria.

The third was that of a woman, aged 80, suffering from hemiplegia of the left side. In eight months' time she had great thirst consequent upon an attack of diabetes. This was followed by gangrene of the right foot, from which she died.

The fourth was that of another woman, aged 39, who in the sixth month of gestation became paralysed, with convulsions. Gradually these disappeared, and only slight swimming in the head remained. Six years afterwards she was found to be diabetic. This patient ultimately died of small-pox.*

Over-mental exertion I have put among the causes of saccharine urine. An interesting example of this kind has recently fallen under my notice in the case of one of our students. During three weeks of mental excitement, sugar was daily detected in his urine. After a fortnight's rest, it entirely disappeared, but recurred a few days after the resumption of the mental labour, again to disappear almost as soon as the labour was discontinued. I have seen again and again mental labour increase the sugar in diabetic patients. In the case of a clergyman, to which I shall subsequently have occasion to refer, on several occasions, I found the daily amount of sugar double itself when he was preparing for his college examinations, and again gradu-

* *Gazette Médicale*, March 14, 1857. For some other cases resultin from cerebral lesions and disease, see *Gazette Médicale de Paris*, March 20, 1858.

ally return to the usual average almost as soon as they were passed, without either medicine or diet being altered.

Irritation of the pneumogastric or of the sympathetic nerves, may give rise to diabetes.

Mr. Nyman relates the case of a professional gentleman who had long suffered from diabetes mellitus. "After we had examined," he says, "the above-named organs (chest, abdomen, and brain), we commenced the dissection of the nervi vagi. On the left nothing abnormal could be found, but on examining the right, we met in the thorax immediately behind the bifurcation of the bronchii a calculous mass (tumour) the size of a hazel-nut, under the entire trunk of the nerve, and appeared to have exercised considerable pressure upon it." He adds that it is the third time that he has met with this morbid condition in persons who have died from diabetes. The urine of this patient contained 6 or 7 per cent. of sugar.*

One case is also recorded in which disease of the sympathetic caused diabetes. In a report of the cases occurring in the Royal Infirmary, Edinburgh, under the care of Dr. Duncan, it is noticed that in one case of diabetes there was found, after death, to be an hypertrophy of the lumbar sympathetic.†

Saccharine urine may also arise as the result of indirect nerve irritation ; thus it is met with in tumours of the abdominal organs and in pregnancy, in which cases the only way to account for it appears to be by the irritation caused by pressure or otherwise of the abdominal sympathetic, perhaps the cœliac plexus or some of its branches.

For further information regarding the effects of nerve lesions and irritation in the production of diabetes, reference must be made to the physiological views previously expressed.

We now come to the consideration of

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* *Dublin Hosp. Gaz.*, from *Swedish Trans.*, July 15, 1857.

† Longet, vol. ii., p. 635.

*Disorders of the Digestive Function as a Cause of Diabetes.*

And, first of all, we must notice those cases which arise apparently from the use of stimulants. It is a well-known fact that cases of diabetes are much more common in Great Britain than on the Continent, and I, like many others, attribute this to the fact of a much greater quantity of alcoholic drinks being used among us than among other European nations. A few years ago (August, 1861), while on a visit to Munich, in the course of conversation, Dr. Pfeüfer, the Professor of Clinical Medicine, told me that he had only had one case of diabetes in the Hospital during the whole six years he had been in Munich; whereas, while Professor in Heidelberg, although the Hospital was much smaller, he had on an average four or five diabetic cases in the course of each year. Now, the only way to account for this difference was, that the Munich Hospital draws its supply from a beer (Bavarian) drinking district, while the Heidelberg Hospital obtains its supply from the wine-drinking districts of the Rhine, etc. And, curious enough, it turned out that even the single case of diabetes Pfeüfer had in Munich, he added, came from the Palatinate.

There can be no difficulty in explaining this action of stimulants, for, as said in the physiological part of the lecture, diabetes can be artificially induced in healthy animals by injecting small quantities of alcohol, ether, chloroform, or even ammonia, into the portal circulation.

For example, I injected ten cubic centimetres of sulphuric ether diluted with thirty cubic centimetres of water into one of the branches of the portal vein * of a full-grown Newfoundland dog half an hour after he had been fed. When he rose up after the operation, he appeared intoxicated, and staggered a little as he moved about. This effect, however,

* The experiment is very easily performed by using a sharp-pointed syringe, which can be pushed with facility through the coats of one

soon disappeared, and in a few hours the animal looked as if nothing had been done to him. In two hours after the injection was made, I passed a catheter into his bladder; but did not obtain sufficient urine to enable me to satisfy myself whether it contained sugar. Some hours afterwards, when I had obtained enough urine, I found that it readily reduced the copper in Barreswil's liquid, thus indicating the presence of saccharine matter. To assure myself that this effect was not due to the presence of any other substance, I boiled the urine in order to coagulate the albumen, of which it contained a little, then evaporated it almost to dryness, dissolved the residue in boiling alcohol, and filtered. The filtered liquid was next evaporated to drive off the alcohol, and an aqueous solution made. On testing the latter for sugar with the sulphate of copper solution, its presence was clearly indicated. Although by this method the existence of saccharine matter was rendered almost undeniable, I still wished to convince myself of its presence by some other means. The urine which the dog passed the next day was therefore fermented, and carbonic acid gas and a trace of alcohol was obtained, thus placing beyond a doubt the existence of sugar.

The following case shows that ammonia has the same power as ether in causing the liver to secrete an abnormal amount of saccharine matter:—

Into the portal vein of a good sized dog in full digestion, I injected fifteen drops of liquor ammoniæ diluted with forty cubic centimetres of water. In twenty hours afterwards, on the animal being killed, his bladder was found enormously distended with urine, which not only reduced the copper in the liquid of Barreswil, but fermented rapidly.

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of the large mesenteric veins. Care must be taken not to employ too much of the stimulant, as it is only up to a certain point that it possesses the power of producing artificial diabetes. If too large a quantity be injected, it seems rather to destroy than increase the glucogenic function.

These two experiments are selected from a number of others, some of which I had the honour of performing in 1853 at the College of France before a Commission appointed by the Société de Biologie; but as the results then obtained are identical it is unnecessary to cite them. I cannot refrain from mentioning with what pleasure I perused a communication of Bernard's, entitled "On the Influence of Alcohol and Ether on the Secretions of the Digestive Canal, of the Pancreas, and of the Liver," read before the Société de Biologie.* M. Bernard, instead of putting the alcohol and ether, as I had done, directly into the portal vein, introduced them, by means of a long œsophagus tube, into the duodenum of dogs, and allowed them to be absorbed through the walls of the intestine, into the portal circulation. The result, as might *à priori* have been anticipated, was identical with what I had previously obtained. Bernard, in fact, found that six centimetres of alcohol mixed with an equal amount of water, was sufficient to excite the liver to secrete a large quantity of sugar, even while the animal was fasting. With ether employed in a similar manner, he obtained no less successful results.

Rosenstein † has still further confirmed the value of the physiological data I obtained, by a very complete series of experiments on the influence of different kinds of drink upon the quantity of sugar, salt, and urea, daily eliminated by a diabetic patient. He performed the experiments, he says, with the view of ascertaining if the conclusions I arrived at were equally applicable to the human subject as to the animals operated upon, and he came to the conclusion that they are identical from his having obtained the following results:—1. Coffee, while it diminished the elimination of urea, increased that of the chloride of sodium and sugar. 2. Bavarian beer had a precisely similar effect. 3. The influence of wine was

* *Gazette Médicale de Paris*, May 10, 1856.

† Virchow's *Archiv.*, 1858, p. 461.

also similar—namely, to decrease the elimination of urea, and augment that of the chloride of sodium and sugar. Lastly, he found that vinegar exerted a similar influence on the elimination of these substances.

If any one doubt the truth of the assertion that stimulants excite diabetes, let him select a case of that form of the disease arising from excessive formation, and after having carefully estimated the daily amount of sugar eliminated by the patient, allow him to drink a few glasses of wine during the next few days, and watch the result. He will soon find that the ingestion of stimulants is followed by an increase of sugar, and if stimulants increase the amount of saccharine matter in the urine of the diabetic, we can easily understand how their excessive use may induce the disease in individuals *predisposed* to it. The effect of stimulants introduced into the portal circulation also explains to us how a disordered digestion is not unfrequently followed by saccharine urine. I may here relate a curious fact in illustration of the latter remark. In 1852, at a time when I was much occupied in studying the physiology of diabetes, I regularly tested my urine twice a-day, and, on one occasion, I found it to contain a small quantity of sugar. On the day in question I had partaken freely of asparagus salad; and, thinking that this might perhaps be the cause of the presence of the sugar, I determined to try the effects of a greater quantity. The following day, the sugar having entirely disappeared from the urine, I again partook of the same kind of salad, both in the morning and afternoon. In the evening, on testing the urine, I found very distinct indications of sugar. As the observation was to me one of great interest, I determined to make some further experiments on the subject, in order to discover how many hours this state of saccharine urine would continue. During two days I ate large quantities of asparagus salad, taking care to have it made as stimulating as possible with vinegar and pepper. The result was far beyond my expectations, for instead of the sugar disappearing from the urine in a few hours after I had ceased partaking of the diet in question, it continued to be secreted during several days, until I at last became very much alarmed lest the disease had been permanently induced. On the evening of the fourth day the sugar had almost entirely disappeared, but on the fifth it returned in increased quantity, so much so that a drop of urine falling on the boot left a distinct white spot. I could not account for the recurrence of the disease, as I had been particularly careful in my diet during the two previous days.

I have mentioned this experiment because it appears to me that if a flow of saccharine urine be induced in a healthy person, as I consider myself to be, by disordering the digestion and over-exciting the liver, it is very probable that a cause insignificant in itself, but operating upon a predisposed constitution, may tend to produce the disease. Sugar in the urine has been found after eating cheese and other indigestible substances. It is worthy of remark that Dr. Jessen, of Dorpat, has rendered horses diabetic by feeding them with hay damaged by moisture. M. Léconte has also found sugar in the urine of dogs after he had administered to them the nitrate of uranium. Several other substances have the same effect, and I have no doubt but that a greater number of stimulants will be afterwards found to produce similar results.

We now come to the consideration of the second form of diabetes—namely, that in which there is no proof of the existence of an *abnormal production* of sugar by the liver, but in which there rather appears to be a *diminished consumption* of the amount normally produced. In illustrating this point I have to rely entirely on clinical data for the opinions at which I have arrived.

It will be remembered that several years ago Piorry communicated to the French Royal Academy a paper, in which he stated that he had successfully treated cases of diabetes by giving the patients sugar-candy, and that he was led to do so from his believing that the cause of death in diabetes is the loss of the sugar which is so necessary to support life. The cane-sugar was therefore given in order to supply the place of the sugar that was lost.

Not long after reading these views, when on a visit at Bristol, Dr. Budd showed me a young man whom he was treating by means of saccharine diet, with apparent benefit. Subsequently, Dr. Sloane(a) and Mr. Amyot(b) published papers on the saccharine treatment of diabetes, expressing similar opinions. On reflecting over the views promulgated by these gentlemen, and comparing them with the results of my own clinical and physiological experience, it gradually occurred to me that there might be two distinct forms of the disease, such as I have already described under the head of diabetes by *excessive formation*, and diabetes by *diminished assimilation;* and further investigation has not only confirmed this view, but enabled me to discriminate between the two classes of cases by the history and appearance of the patients alone. Before giving examples of each form of the disease, let me first explain one or two things regarding the symptoms of diabetes, which, I fear, are but imperfectly understood.

First, as regards the amount of urine eliminated, some appear to consider it a most important sign, and one which we should try and check as soon as possible. Now, I beg to differ from them, for I believe it fortunate that the diabetic patient does pass an excess of water.

The excessive elimination of sugar is not consequent upon the increased flow of urine, for we may have, as already seen, an excessive flow of urine without sugar,—but exactly the reverse; the excessive flow of urine is consequent on the elimination of the sugar. The sugar, in order to be eliminated,

(a) *Brit. Med. Jour.*, March, 1858.
(b) *Med. Times and Gaz.*, March, 1861.

must be dissolved, and, in order to be dissolved, must have water, and the more water the more readily does the elimination of the sugar take place. Some may say, we want to stop the elimination of the sugar. Not so; we want to stop the disease inducing it,—not the elimination of the sugar, which is the mere result of the disease. Retaining the sugar in the blood would only tend to hasten the death of the patient by still further deranging the nutritive functions, and causing an abnormal diasmose by altering the relative specific gravity of the blood and other secretions. Remove the cause of the accumulation of saccharine matter in the blood if you can, but if you cannot do that, aid, instead of trying to retard, its elimination from the body.

Diabetic patients generally pass more liquid than they take—about one-fifth or one-quarter more—and although they ought never to drink more than they feel a want for, yet they must never be stinted, for their continual thirst is but nature's cry for relief. If the patient did not drink, the blood would soon get too thick to circulate freely through the vessels, and a variety of secondary diseases would be induced. Stopping the drink diminishes the elimination, but does not stop the formation of the sugar. When the formation of sugar decreases, the urine of its own accord becomes diminished.

As regards the amount of sugar eliminated, which is generally considered an infallible criterion of the condition of the patient, experience has shown me that such an idea is erroneous. A diminution in the sugar in cases from *excessive formation* is always a good sign, but in those arising from diminished assimilation it is, on the contrary, occasionally the reverse. Thus I have again and again seen patients who were gradually succumbing from the starvation effects of a restricted diet, at once pull up and improve on a judicious mixture of vegetable food, notwithstanding that the amount of sugar in the urine was thereby greatly increased. It is the weight of the patient, not the quantity of eliminated sugar, on which we ought to rely in such cases.

Although advocating the employment of vegetable diet in cases of diabetes of the second class, I do not wish it for a moment to be supposed that I agree with Piorry in thinking that the cause of death, even in this form of diabetes, arises from the loss of sugar ; for, on the contrary, I think it springs from the inability of the body to assimilate the sugar it possesses. In such cases, therefore, I give vegetable food, not because it contains sugar, but because it possesses many of the other substances necessary for the purposes of nutrition, which neither exist in the same quantity nor in so easily an assimilated form in animal diet.

It is well known from the reports of travellers among savage nations. that men restricted solely to animal diet must consume an almost fabulous amount in order to obtain sufficient of all the ingredients requisite in the processes of life. We know, too, that an animal can be most effectually starved by limiting him to one particular element of food, although that element be even albumen.

The benefits derivable from Piorry's plan of treatment, therefore, in my opinion, arise from the fact that when he gives sugar he at the same time ceases to restrict the patient to animal diet, and that in the mixed food they find many of the materials essential to life much more abundantly and in a more easily assimilated form than in animal diet.

I shall now give a few typical cases illustrative of the two principal forms of diabetes.

### *Diabetes from Excessive Formation.*

In the beginning of 1860 a young gentleman, aged 19, suffering from diabetes, was brought to me by his brother, a Medical Practitioner, who had detected the disease two years previously. This patient had already been under various systems of treatment. What appeared to agree with him best was animal diet, coupled with small doses of chlorodyne. To look at the patient one would have thought that he was a perfectly healthy individual. His weight was 135 lbs.; the appetite was moderate; and the amount of urine passed was not at that time excessive. The object of bringing the patient to me, it appeared, was in order that I might, if possible, suggest some remedy to replace the chlorodyne, the constipating effects of which were anything but agreeable. On carefully inquiring into the history of the patient, the case appeared to be one of diabetes by excess, and the origin of the mischief could in some measure be traced to some irritation in the liver, which was painful at its lower margin, the pain being much increased on pressure. Having an intelligent Practitioner to deal with, I at once gave my view of the case, and explained how, as scarcely any two cases of diabetes are precisely alike, it would be necessary to try the effects of different forms of treatment in order to discover what would be best for this particular case.

The following table is an abstract of the results :—

| Date. | Quantity. | Sp. gr. | Sugar. | Urea. | Weight. | |
|---|---|---|---|---|---|---|
| 1860. | | | grms. grs. | grms. grs. | lbs. | |
| March 27. | 1980 | 1026 | 99·05=1535·27 | 45·50=705·25 | 135 | Animal diet; ordinary bread; 5—6 glasses of wine and chlorodyne. |
| April 10 . | 1680 | 1034 | 129·24=2003·22 | 36·96=572·88 | — | On the same diet and drink as above, but no chlorodyne. |
| April 20 | 1680 | 1034 | 93·33=1446·61 | 50·40=781·20 | — | Animal diet: gluten bread and wine. |
| May 13 | 2085 | 1024 | 79·49=1232·09 | 57·26 887·53 | — | Animal diet and gluten bread, without wine or medicine. |

| Date. | Quantity. | Sp. gr. | Sugar. | Urea. | Weight. | |
|---|---|---|---|---|---|---|
| August . | 2010 | 1023 | 87·39=1354·54 | 46·33=718·11 | — | Animal diet and gluten bread, one glass of wine, and ext. conia.(a) |
| December | 1860 | 1022 | 90·00=1395·00 | — | 149 | Same diet and treatment as last. |
| 1861. January . | 1798 | 1024 | 119·20=1847·60 | 35·96=557·38 | 154 | Diet the same as before, but part of the conia (6 grs.) replaced by ¼ gr. of belladonna. |
| February . | 1736 | 1026 | 157·82=2446·21 | 34·70=537·85 | — | On ordinary diet and without medicine. |
| March . | 1798 | 1037 | 224·66=3482·23 | 46·51=720·90 | — | Still on ordinary diet and without medicine. |
| July. . | 1675 | 1031 | 83·75=1298·12 | 50·25=778·87 | — | On animal diet, gluten bread, and cannabis indica. |
| November | 1829 | 1026 | 61·30= 950·15 | 25·74=398·97 | — | Diet as before; medicine a mixture containing conia, cannabis indica, and hydrocyanic acid. |
| December | 1736 | 1028 | 49·91= 773·60 | 39·92=618·76 | — | Do., do. |
| 1862. July. . | 1736 | 1030 | 57·60= 892·80 | 58·31=903·80 | — | Do., do., but less restricted diet. |

The average amount of sugar passed by this patient during the next six months being from fifty to sixty grammes (775 to 930 grains) and his weight 156 pounds, a quantitative analysis of the sugar was no longer thought necessary. I may add that when I last saw the gentleman in August, 1864 (on the occasion of his bringing to me a poor lad, whose case I shall presently relate), he looked in excellent health, being, as he said, without any feelings of discomfort, although he had still to continue his medicine, for as soon as he neglected it, the sugar again increased.

(a) As many of the preparations of conia are utterly valueless, in consequence of their containing little or none of the active principle, that given was first tested on frogs before being employed.

The next case is that of a lady who also suffers from diabetes by excess. Before coming to me she had been under a gentleman connected with one of the City Hospitals, who treated her according to what has been hitherto considered the orthodox principles of restricted diet, upon which treatment she had thriven so well that when she walked into my consulting-room I never dreamt that she came to talk about herself, but imagined she came about the health of another patient with whom she had been to see me a short time previously. She looked, in fact, the very picture of health; being plump, hale, and rosy.

Like many patients in her position of life, she thoroughly understood the nature of her disease, and criticised the opinions of our first authorities on the subject in a manner which somewhat surprised me—especially when she finished by saying she had come to put herself under my care, not for the purpose of being dieted, *but for the purpose of being able to live without being dieted.* She was tired, she said, of gluten bread, etc., and wanted to live like other people. She had brains enough to see that dieting kept down the sugar, not by curing the disease, but merely by stopping the supply, and that as soon as she gave up the restricted diet, back came all the disagreeable symptoms.

On analysing the urine I found she was in as good a condition as restricted diet could make her; the quantity of urine passed was moderate, of a specific gravity of 1030, and the amount of sugar comparatively trifling,—310 grains. Diagnosing the case to be one of diabetes by excess, I honestly told her that although her case was one of the most favourable as far as longevity was concerned, it was one of the least satisfactory kind to put on ordinary diet. At the same time adding, that the treatment must, in the first place, be entirely experimental, it being impossible to say what remedy would most successfully allow her to dispense with dieting.

The case so closely resembled the preceding in its general characters, that I ventured on the same line of treatment, and, as will be seen by the subjoined table, with a favourable result. The sugar gradually diminished, until at length, after seven months' treatment, the saccharine matter had entirely disappeared from the urine.

Being too sanguine as to the result, in an unlucky moment I consented to the patient's throwing aside the restricted diet, and whether this was done too suddenly or not I cannot say, but certain it is, that before a month was over, the urine contained as much, and even more sugar than when first I took the case in hand.

| | Quantity. | Sp. gr. | Sugar. | Urea. | |
|---|---|---|---|---|---|
| 1863. | | | grm. grs. | grms. grs. | |
| December | 1860 | 1030 | 20·00=310·0 | — | On animal diet and gluten bread; no other treatment. |
| 1864. | | | | | |
| January . | 2480 | 1022 | 5·00= 77·5 | 81·84=1268·52 | After taking conia and cannabis Indica during fourteen days; animal diet and gluten bread, as before. |
| March . | 1830 | 1030 | 4·23= 65·5 | 78·56=1217·68 | Do., do. |
| April . | 1674 | 1023 | 2·10= 32·5 | 50·22= 778·41 | On the same diet, but, after increasing the narcotic by one-third (40♏), during last three weeks. |
| May . | 1395 | 1030 | Too little to calculate | 69·75=1081·12 | Same as last, but has been occasionally indulging in a very small piece of ordinary bread. |
| June . | 1178 | 1030 | Only a trace | 44·76= 693·78 | Diet still restricted; has once or twice indulged in a potato at dinner; takes the medicine as before. |
| July. . | 1364 | 1016 | *None* | 39·55= 613·02 | Has had one meal a-day of ordinary diet during last ten days. |
| August . | 1984 | — | 20.60=319·3 | 59·50= 922·25 | After being for nearly a month on ordinary diet. |
| November | 1550 | 1030 | 13·00=201·5 | 74·40=1153·20 | Restricted diet and medicine as at first. |
| December | 1488 | 1026 | 10·00=155·0 | 52·08= 807·24 | Do., do. |

One very remarkable peculiarity of this case is the very large amount of urea passed by the patient. A large quantity of urea is common to all diabetic cases, and especially to those on animal diet. Regarding the cause of the high percentage of urea in diabetes, the Rev. S. Haughton (a) remarks that it comes from the excessive decomposition of protein substance which takes place in this disease, quite independent of the amount of bodily work done.

In a series of observations on two cases in University College Hospital, Ringer(b) arrived at the following conclusions :—

1st. That after the influence of food on the urine has entirely disappeared, a constant ratio is maintained between the sugar and urea.

2nd. That after a purely non-amylaceous and non-saccharine meal both the sugar and urea are increased, but that during this increase the same ratio between them is observed. This ratio being 1 of urea to 2·2 of sugar.

3rd. That under both these circumstances the sugar could only be derived from the nitrogeneous elements of the body, and, therefore, that some such ratio might, on *à priori* grounds, have been expected.

*Diabetes from Diminished Assimilation.*

We shall now take examples of diabetes due to *diminished assimilation*, and for this purpose select two cases from Hospital practice, for the reports and analysis of which I am entirely indebted to the combined labours of our clinical clerk, Mr. Joseph Thompson, and my class assistant, Mr. J. S. Cluff.

One male and one female patient are again selected, and that too of as near as possible parallel ages to the preceding cases of the disease by excessive formation, so that the comparison of the results may be facilitated.

Fredk. F., aged 16, admitted into University College Hospital on October 15, 1864. Father and mother both living

(a) "Phenomena of Diabetes Mellitus." Dublin. 1861.

(b) "On the Relative Amount of Sugar and Urea in the Urine of Diabetes Mellitus." *Trans. Med.-Chir. Soc.*, 1860, p. 323. *Year-book*, vol. II.

and healthy; family history generally good; no history of phthisis. Present illness commenced about a fortnight after last Easter (March 27), when patient first noticed that he made a great deal of water—six or seven pints daily—was very thirsty and drank much. His appetite was also very great; says "he used to eat anything that came before him." Has been treated dietetically, and, his father being a butcher, has had plenty of animal food. He improved for a time, but soon fell off again, and has been gradually getting worse; is much emaciated; used to weigh 105 lbs., but now only weighs 75 lbs.; skin very rough and dry; bowels regular; chest sounds healthy; no pain, cough, or night sweats.

The diagnosis of the case being of diabetes from mal-assimilation, the patient was placed on ordinary diet, including common bread, eggs, and a pint of beer; while to improve his general health a mixture with phosphoric acid and strychnine was ordered.

The patient's temperature was noted three times a day from October 19 to November 3, and found to average 97⅘° F., being three degrees below the ordinary standard.(a)

November 25.—Patient looks better. Says "he feels himself much improved; is not so thirsty; and makes less water." Goes home into the country to-morrow.

The following table shows the results of the analysis.

| Date, 1864. | Quantity of Urine in cub. cent. | Reaction. | Sp. gr. | Quantity of of Sugar in grammes. | Urea. | Weight in pounds. |
|---|---|---|---|---|---|---|
| October 21 .. .. | 3480 | Neutral. | 1040 | 218·00 | — | 75 |
| ,, 26 .. .. | 5457 | ,, | 1037 | 286·10 | — | 77 |
| ,, 28 .. .. | 7000 | Acid. | 1033 | 280·00 | — | 77 |
| ,, 31 .. .. | 6200 | ,, | 1034 | 281·18 | — | 80 |

(a) Rosenstein was, I believe, the first to mention that in diabetes the temperature of the body is below the normal standard (*Virchow's Archiv.*) I find, however, that this is only invariably true in that form of the complaint arising from mal-assimilation.

| Date, 1864. | Quantity of Urine in cub. cent. | Reaction. | Sp gr. | Quantity of Sugar in grammes. | Urea. | Weight in pounds. |
|---|---|---|---|---|---|---|
| November 4 .. .. | 6508 | Acid. | 1037 | 260·8 | — | 78 |
| ,, 7 .. .. | 6660 | ,, | 1037 | 281·16 | 39·960 | 80 |
| ,, 9 .. .. | 6700 | ,, | 1036 | 341 6 | 40·200 | 80 |
| ,, 16 .. .. | 6840 | ,, | 1036 | 348·12 | 44·460 | 79 |
| ,, 18 .. .. | 5860 | Neutral. | 1034 | 322·17 | 41·020 | 79 |
| ,, 22 .. .. | 5790 | ,, | 1033 | 246·5 | 49·215 | 79 |
| Received urine from the country: | | | | | | |
| December 2 .. .. | 6300 | — | — | 187·29 | — | 84 |
| ,, 22 .. .. | 5735 | Feebly acid. | 1035 | 248·8 | 57·35 | 87 |
| 1865. | | | | | | |
| January 26 .. .. | 5890 | Acid. | 1036 | 294·5 | 44·17 | 90 |
| February 22 .. .. | 5270 | ,, | 1035 | 263 5 | — | 90 |
| April 11 .. .. | 5580 | ,, | 1031 | 134·2 | 40·65 | 90 |

During the first few days after the patient's admission into the Hospital the quantity of the urine was greatly diminished, but as he became accustomed to the change, it again rose to its average, and there remained until tinct. of cannabis Indica along with four drops of laudanum three times a day was administered (November 16), when it immediately fell 1000 cub. cent. in the twenty-four hours. The quantity of sugar eliminated also decreased, but of course, in consequence of the nature of the case, not to any marked degree. The patient, since his return to Nottinghamshire, has still continued the use of the remedy, the effects of which will be best appreciated if I quote a passage or two from the last letter he wrote to Mr. Joseph Thompson, dated April 10, 1865 :—" I have sent you another sample of my water. . . I am a great deal better in health and strength, and my weight is 90 lbs. without my clothes. I am still taking Dr. Harley's medicine, and with thanks," etc., etc.

The rapid improvement which took place in this case when the diabetic system of treatment was discontinued, and the patient was put back to ordinary food, is not a little remarkable. The improvement cannot be attributed to the change of air or mode of life, for as we see it continued just the same when the lad had returned to his own home and former avocations. This is a most instructive case in more respects than one, for had the patient been treated by the ordinary routine system, the more sugar he passed, and, consequently, the worse he became, the more restricted would have been his diet; and I have little hesitation in saying that had such a line of treatment been pursued it is highly probable that ere now the case might have terminated fatally, for, as before said, at the time the lad came to the Hospital he was but a shadow of his former self, having lost 30 lbs. in a few months.

I have now to contrast a case of diabetes arising from malassimilation in a female with that from excessive formation in the lady's case previously cited. The nearest in age happens to be a very bad case—I may say a hopeless one, for the disease was much too far advanced before the girl came to the Hospital to render it probable that she will ultimately recover.

Sarah F., a milliner, aged 27, single, was admitted into University College Hospital on January 23, 1865. Has been an out-patient under Dr. Harley since December 9, 1864.

*History.*—Father died of "dropsy;" mother living (aged 72), has always had good health; has five brothers and sisters all healthy; no history of phthisis in the family. Patient states that until the last twelve months she has always enjoyed very good health; about this time (twelve months ago) she began to feel weak, and had a general feeling of *malaise;* she lost her appetite, and since last August (when she weighed about nine stone) has lost three stone weight. Three or four months ago, a few days after receiving a great mental shock, she first noticed that she made a great deal of water (five pints in twenty-four hours); she could eat nothing at this time, but was excessively thirsty, and used to drink large quantities of milk and toast water; lived chiefly on slops, arrowroot, &c.; took no solid food whatever; says "she has not moisture enough in her mouth to swallow." Her appetite since she has been an out-patient has materially improved. Still thirsty. Patient is tall, but very thin; skin dry, harsh, and rough; lips dry; flush on cheeks; no cough or night sweats; does not sleep well of a night, but has no pain; bowels very costive, will not act without medicine. Has not menstruated since last August, but up to that time her courses had come on too frequently—every fortnight or three weeks irregularly. Urine very light coloured; sp. gr. 1041; no albumen, but abundance of sugar.

Put on ordinary bread diet, including chop, beef-tea, milk, custard pudding, brandy ℥ij.

Before coming under Dr. Harley's care the patient had been treated dietetically.

From December 12 until February 10, the patient took fifteen minims of tincture of cannabis Indica three times a day. She left the Hospital and became an out-patient again at her own desire.

| Date. | Quantity. | Sp.gr. | Reaction. | Sugar. | Urea. | Weight. |
|---|---|---|---|---|---|---|
| | c. c. | | | grms. grs. | grms. grs. | lbs. |
| Dec. 10 | 3720 | 1037 | Acid | 186·00=2883 00 | 53·80=833·90 | 81½ |
| ,, 12 | 3642 | 1037 | Neutral | 214·20=3320·10 | 58·27=903·18 | 83 |
| ,, 16 | 3562 | 1036 | Acid | 178·25=2762·87 | 60·30=934·65 | 85½ |
| ,, 23 | 3720 | 1035 | — | 150·80=2337 40 | — | — |
| Jan. 4 | 3825 | 1040 | Neutral | 161·45=2502·47 | — | 86 |
| ,, 7 | 2790 | 1038 | Neutral | 116·25=1801·87 | — | — |
| ,, 17 | 2945 | 1032 | Acid | 98·16=1521·48 | 55·95=867·22 | — |
| Feb. 7 | 3038 | 1038 | — | 138·0 =2139·00 | — | — |
| ,, 10 | 3317 | 1034 | — | 144·50=2239·75 | — | — |
| ,, 18 | 2697 | 1039 | — | 134·10=2078·55 | — | 87 |
| March 6 | 3100 | 1033 | Acid | 129·15=2001·82 | — | — |

Mr. Cluff informs me that in both this and the preceding case the analyses were always made on a sample of the forty-eight hours' urine, consequently the results are of double value. No one will, I think, venture to say any of these cases have been selected on account of their being favourable specimens for treatment, for in reality they were just the reverse.

Both of the two last cases had been considered perfectly hopeless by their respective Medical attendants, and yet we see that under a different line of treatment they both improved. The first one may ultimately get well; the last I am not sanguine about, notwithstanding that the strength of the patient has considerably improved. When first brought to the Hospital, the girl was so weak as to require to be allowed a seat during her examination; whereas at her last visit she said she was able to walk to the Hospital, a distance of more than a mile; but even that distance seemed to knock her up. There are three bad features in her case:—Firstly, the want of appetite; secondly, the excessively costive bowels; and thirdly, the large amount of urea passed considering the small quantity of food taken.(a) These four last-mentioned cases, I think, clearly illustrate the difference between diabetes resulting from *excessive formation*, and diabetes arising from *diminished assimilation*. I have only now once more to remark that as far as dieting is concerned, the treatment of the two classes of cases is diametrically opposite. The chance of success will therefore be in direct proportion to the correctness of diagnosis.

It ought always to be borne in mind that there are such things as *acute*, as well as, *intermittent diabetes*. First, as regards the acute form of the disease.

*Acute Diabetes.*—Two remarkable examples of this kind are reported by Dr. Noble.(b) One case was that of a boy aged 17, who died three days after the disease was discovered, and only a few weeks after he first felt ill. The other, a young lady, who died on the tenth day after the nature of her malady had been diagnosed.

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(a) I have since heard from Mr. Clarke, of Gerrard-street, that this poor girl subsequently died while under his care, the most striking feature of her case being the impossibility of getting the bowels to act.

(b) *Brit. Med. Jour.*, Jan. 17, 1863.

*Intermittent Diabetes.*—In some patients, again, the peculiar condition of body inducing saccharine urine is not in constant operation, but comes and goes at irregular intervals. A well-marked case of this kind occurred in the practice of Dr. Ramsbotham, of Amwell-street, the particulars of which he has kindly furnished to me. They are as follows :—

"A lady, aged 72, applied to me in September, 1860, in consequence of sore tongue and intolerable thirst, which at that time had existed for several weeks. The peculiar smell of the breath and increased quantity of the urine (four or five pints each day), induced me to suspect diabetes. On examination, I found the specific gravity to be 1044, obtained a deep brown colour on boiling with caustic potash, and a copious red precipitate with sulphate of copper and potash. I gave mineral acids, with generous diet, omitting, as far as possible, all farinaceous food. By the end of a fortnight the specific gravity of the urine was under 1020, and without a trace of sugar. At the end of another fortnight the specific gravity became again 1044 and the urine loaded with sugar. This intermittent state continues up to the present period. The specimen of urine for the last twenty-four hours (November 26, 1861) has a specific gravity of 1018, and does not contain sugar."

### *Diabetes complicated with Other Disease.*

Having already seen how saccharine urine is frequently the result of other affections, I have now to point out how other diseases frequently arise from the want of stamina induced by the diabetic diathesis. This is more particularly the case with that form of affection resulting from defective assimilation, in which, to use an insurance office expression, "it is a bad life." As I said before, Prout used to say of all diabetic patients, that they perpetually stood on the brink of a precipice. That statement, though still perfectly true, has been fortunately stripped of some of its terrors, since physiology has taught us that, under judicious treatment, the life of the diabetic may be made little inferior to that of patients labouring under other chronic affections. Forewarned in this disease is truly forearmed, so if the patient neglects the warning he has but himself to blame for it.

Some few affections seem to be the direct effects of an excess of sugar in the circulation, others the indirect result of the low condition the excess induces, rendering the body unable to resist the inroads of disease. Thus Mr. France has called attention (a) to the frequency with which cataract is met with in the diabetic, and relates cases of its occurrence at an early age—30, and even 19 years. The characters of these cataracts are peculiar,—Firstly, they are symmetrically developed on both sides; secondly, the lenses are increased in the antero-posterior diameter, so as to interfere with the free play of the iris; thirdly, the opacity attacks different strata of the lens at once; fourthly, the colour and bulk of the lens denotes its soft consistency; and, lastly, they do not come on till after the renal malady has existed for some considerable time. Moreover, the eye ought in no case to be interfered with, unless the patient is completely blind, as these cases are not good for operation.

The cause of these cataracts has been well explained by Dr. Richardson,(b) who was able to produce them artificially in animals. They arise from a physical cause—osmose—a tendency to equalise the density of the fluids in the lens with those exterior to it,—in fact, the imbibition of sugar and the transudation of liquid from the lens. Chloride of sodium and other saline solutions produce the same effect. They are not, indeed, true cataracts, and the proper treatment is to cure the

(a) *Dub. Hosp. Gaz.*, May 1, 1859, p. 136.

(b) *Med. Times and Gaz.*, March 31 and April 21, 1860.

diabetes, not to extract the lens, which will become quite right of itself when the quantity of sugar in the circulation is reduced.

Cases of diabetes are occasionally complicated with albuminuria. In some instances the kidney disease supervenes in the course of the diabetes. One such case has already been mentioned; another occurred to myself. The diabetic patient, a man forty years of age, was suddenly attacked with albuminuria and dropsy after exposure to cold and wet. The albuminuria, after a time, gradually disappeared; the dropsy likewise diminished, but the saccharine state of the urine remained. On the other hand saccharine urine occasionally makes its appearance in the course of albuminuria. This I have frequently seen; but then, the diabetic condition was not only trifling, but merely temporary, so that little importance need be attached to it. It may, however, become permanent, in which case, especially if the patient is aged, great fears for his safety are to be entertained. I shall presently relate a fatal case of this kind; meanwhile, I may mention a most interesting one which recently occurred in the practice of Dr. Eastlake. The patient, a young gentleman aged 12 years, had resided for a time at Calcutta. His urine, when I examined it, was four ounces in quantity, had a specific gravity of 1012, was highly albuminous, giving a copious precipitate with heat and nitric acid, either separately or combined, and contained a considerable quantity of sugar. The urine, when boiled with potash, became brown, and gave off the odour of glucic and melassic acid. With sulphate of copper and potash, on the other hand (it mattered not which of these solutions was added first), a fine mauve, instead of a blue, liquid was obtained. On boiling, the mauve, as is usual in those cases, changed to a purple, then to a red, and lastly, a considerable quantity of sugar being present, a precipitate of the reduced oxide of copper was thrown down.

On questioning the patient and friends closely regarding the origin of the disease, nothing more could be elicited than that his legs began to swell about two years ago, and that on his urine being tested, it was found to be albuminous, there being not the slightest history of nephritis, either with or without scarlet fever.

On carefully examining the abdomen the liver was found to be enlarged (3½ inches perpendicular to nipple), and tender on pressure. This led me to the idea that the albuminuria was secondary to the hepatic affection. As regards the sugar, I may mention that it does not seem to have been discovered until the patient came under the care of Dr. Eastlake, which was some weeks previous to our consultation.

The reason why I said that when sugar permanently appears in the urine in the course of albuminuria fears for the safety of the patient are to be entertained, is because it generally indicates a loss of vital energy, which, sooner or later, leads to a fatal termination. Dr. Quain has communicated to me an interesting case of this kind. The sugar first appeared three years after the albumen. The amount of the urine passed shortly before the patient's death being ten pints, and the specific gravity, in spite of the albumen, 1035.

It may be laid down as a rule, as I have elsewhere(a) pointed out, that the supervention of permanently saccharine urine, even when the amount of sugar is very small, in the course of *any chronic disease*, is invariably to be regarded as a most unfavourable symptom. It is not at all improbable that cases of albuminuria and diabetes may be met with in the human subject when these morbid affections are the simultaneous result of nerve lesion. The reason I think so is, that I, like every other experimental physiologist who has worked much at this subject, have occasionally induced both albuminuria and diabetes in puncturing the fourth ventricle of animals.

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(a) "On Jaundice and Diseases of the Liver," p. 70.

This accident has generally happened when the injury to the nerve substance has been made too high up.

A curious case of cancer of nearly all the viscera, conjoined with albuminuria of one kidney and saccharine urine of the other, has been reported by Dr. Gibb,(a) the history of which is as follows :—

A woman, aged 55, had been affected with cancer of the uterus for four years, and three years before two operations were performed for its removal. The disease, however, returned, and destroyed the neck of the uterus, the anterior wall of the vagina, and posterior part of the bladder, the urine dribbling from this general cavity for upwards of a year. She died on October 13, the left leg being in a state of gangrene. On examination after death, the lungs, pleura, and bronchial glands were found affected with cancer, the former containing distinct tuberculous masses as well, some as large as an egg. The liver weighed four pounds, and contained a number of circular cancerous tubercles. The spleen also contained a cancerous nodule. The right kidney weighed, with the fluid contained in its dilated pelvis, seven ounces and three-quarters; the left, much smaller, weighed, with its fluid, three ounces. From both extended dilated ureters filled with urine. The urine in the larger kidney was of the specific gravity of 1026, feebly acid, and contained sugar, as proved by the usual copper and other tests; that in the left was of the specific gravity of 1015, neutral, and contained much albumen. The condition of the urine had unfortunately not been previously ascertained, as none could be obtained from the bladder during the last nine months of the patient's life.

Diabetes may also be associated with chylous urine. From the observations of Dr. Babington,(b) indeed, it might almost

(a) Path. Soc. *Trans.*, 1859.

(b) Todd's "Cyclopædia of Anatomy and Physiology:" article by Dr. Babington on the morbid conditions of the blood.

be concluded that a saccharine condition of the blood predisposes to this disease, for many of the patients suffering from diabetes whose blood Dr. Babington examined were found to be suffering from that condition called piarrhœmia (milky serum).

A few years ago I had the urine of one such patient sent to me for analysis by Dr. Charles Coote. The case, which was afterwards published by that gentleman, (a) was more than usually interesting, in consequence of its origin having been traced to psychical causes (mental anxiety), and from its having run a very rapid course. The ordinary symptoms of diabetes, such as thirst, and excessive flow of urine, only existed for three weeks. The average amount of water daily passed during that time was from five to six pints, and of a specific gravity of 1031·34.

It has already been said that diabetes is often associated with two forms of inflammation. Boils and dangerous carbuncles are well known frequently to accompany it; and now it would appear from a paper in the *Union Médicale* of February 28, 1861, that even gangrene occasionally arises in the later stage of diabetes. This is not at all incomprehensible, seeing the great derangement to the process of interstitial nutrition to which a supersaturated saccharine state of the blood gives rise.

Lastly I have to call attention to impotence as a common accompaniment of diabetes, especially in men nearing or a little beyond the prime of life. Before me is the urine of a case of this kind now under treatment at the Hospital. The man, J. W., aged 50, was sent to me a few months ago on account of diabetes. This case having been a very favourable one of defective assimilation, under a course of zinc as a tonic, the saccharine urine may be said to have entirely disappeared. At least, the sugar is now in such small quantity that for the

(a) *Lancet*, September 8, 1860.

last six weeks it has not been considered worth the trouble of a quantitative analysis. Indeed, on the last occasion (two months ago) that a quantitative analysis was made, Mr. Cluff found it amount to only 1·2 grammes (18½ grains) in the twenty-four hours' urine. The patient is at present being treated for the impotence which began shortly after he discovered that he was diabetic, which is now six months since. During this period he has never had an erection, although he has several times had emissions during his sleep.

Cases of this kind are not uncommon; fortunately, however, there is one good thing connected with them—namely, that after the saccharine urine is stopped the steady employment of a strong nervine tonic, such as strychnine, is generally sufficient to effect a cure.

*Treatment.*—Like all intractable maladies, diabetes has had a great many specifics proposed for its treatment, and this is not surprising, seeing that the number of specifics generally increase in exact proportion to the irremediable character of the disease they are proposed to cure. I am not, therefore, going to take up time by even attempting an enumeration of the names, far less of the vaunted virtues, of the specifics for diabetes, but shall at once proceed to lay down a few of the general principles upon which my own line of treatment is founded.

Fortunately, medicine is of much use in this affection; and although some cases, of course, are beyond all human aid, yet many—I might almost venture to say the majority—are, to some extent, under our control; and although no one would venture to say that he can remove the malady, yet in almost every case we can substantially mitigate the more distressing of the symptoms, and render the patient comparatively comfortable for the remainder of his life. Occasionally we have the satisfaction not only of finding the symptoms improve under treatment, but even the saccharine condition of the urine entirely disappear. We must never, however, speak too sanguinely even of such a case, for a person who has once had diabetes is far from being in the same condition as one who never suffered from the disease ; for, just as with insanity, no matter however perfect the lucid interval may be, there ever exists the danger of a relapse, so with diabetes, however long the intermission may be, there always remains the danger of a return of the affection.

The two great types of diabetes, that due to *excessive formation*, the other to *diminished assimilation* of saecharine matter, require, of course, as far as animal dieting is concerned, opposite modes of treatment; for while in the former class of cases it is a most important—I might almost say an essential—adjunct to the other treatment, in the latter it is either detrimental, or, at best, of no use at all.

Even in the most favourable cases for restricted diet, we must never allow ourselves to be deluded into the idea that, because we are mitigating the symptoms, and reducing the amount of sugar in the urine, we are neeessarily curing the disease, or we shall frequently be doomed to sad disappointment. In keeping a patient on restricted diet, we are merely withholding from him the straw and mortar out of which the bricks are made—not removing the makers—so that, as soon as the straw and mortar is refurnished to them, they will again be found at work as actively as ever. It is true that it occasionally happens during the withdrawal of the straw and mortar the makers disappear; but this, unfortunately, is by no means invariably or even frequently the case; it is rather, indeed, the exception than the rule. We must therefore rely on other means for the removal of the makers. Of these other means I shall presently speak. Meanwhile, let me explain that by the term restricted diet we mean not only the avoidance of all sugars, and substances containing saccharine matter, but also of all kinds of food eonvertible during the process of digestion into sugar. The foods convertible into sugar in the digestive canal are those containing starch (not gums), such as arrowroot, tapioca, sago, flours of all the different kinds of cereals (wheat, barley, oats, peas, beans, etc.), potatoes, carrots, beetroot, parsnips, turnips, and other edible roots.

Green vegetables, on the other hand, such as spinach, cabbage, turnip tops, Brussels sprouts, and lettuce need not be forbidden, as they contain too small an amount of starch to do much injury.

As for animal foods, on the other hand, every imaginable kind of fish, flesh, and fowl may be indulged in, so that even on the most restricted diet the patient has still a large margin for selection—beef, mutton, pork, venison, poultry, game, and wild fowl, oysters, lobster, crabs, prawns, salmon, cod, turbot, etc., Iceland and Irish moss, calf's foot or gelatine jellies, butter sauces, and salad oils. The only true hardship, in fact, the patient suffers is the deprivation of ordinary bread, and that appears to be a more severe one than most people imagine. I have known patients in whom the craving became at last almost intolerable, as if nature were crying out for some indispensable element of food. In order to mitigate this hardship, a great number of plans of depriving bread of the forbidden element, starch, have been suggested, and many of them have been in a great measure successful. Thus, we have bran, gluten, almond, and glycerine breads and biscuits constantly kept in stock by many of our London bakers.(a)

After a time patients get very tired of these substitutes, so it is as well to know that we may occasionally indulge them with well done toast, or very crisp pulled bread, the extra

(a) Blatchley's, 362, Oxford-street, N.; Donges, Gower-street North, W.C.; Hill and Son, 61, Bishopsgate-street, E.C.; Van Abbotts, 5, Princes-street, Cavendish-square, W. Persons in the country or any others who may desire to have the bread made at home may obtain pure gluten flour daily or weekly from Parsons, Fletcher, and Co., 22, Bread-street, E.C.

heat having destroyed a considerable portion of the starch normally contained in the article.

As regards drinks, all such as contain saccharine matter are to be avoided; such, for example, as sweet sparkling wines, whether they be champagnes, moselles, or hocks. An embargo is also to be put on all liqueurs and fruity wines, such as young port, Roussillon, etc.; sweet ales, stout, and porter are also to be shunned. If the patient is to be indulged in wines at all, let him have dry Lisbon, old Madeira, Manzanilla, or Amontillado sherries, Chablis, Niersteiner, or old Sauterne; sound clarets may also be indulged in. When stimulants are deemed requisite, brandy, whisky, rum, or Hollands may be used; but these ought always to be employed with caution for the reasons previously given, when speaking of the artificial production of diabetes by means of stimulants introduced into the portal circulation.

All that has now been said regarding regimen has of course only had reference to that form of diabetes arising from *excessive formation*. There are no restrictions either as regards food or drink requisite in cases springing from *defective assimilation*. On the contrary, the duty of the Practitioner is to select for his patient not only that which is most nourishing, but also that most easy of assimilation. He will often find, too, that such cases not only tolerate but even demand the free use of stimulants, in order to support the flagging vital energies, and enable the weakened organs to perform their work. I think if I were asked what is the best remedy for diabetes, I might venture to answer, in the language of Opie, when the student inquired what he mixed his colours with, "BRAINS, SIR." For to say that any one remedy or particular line of treatment is suitable to all cases of diabetes would be simply charlatanism of the worst sort.

For example, when diabetes arises from a traumatic lesion of the nervous system, it is not the symptom of saccharine urine that we treat. It, we know, will disappear when the nerve-lesion is healed. All our energies are, therefore, directed to the hastening of the healing process.

On the other hand, when the cause is not traumatic lesion, but disease of the nervous system, which we know is neither likely to disappear of itself nor by treatment—such, for example, as tumour of the pneumo-gastric nerve—our efforts are directed to the subduing of its effects.

A similar remark is equally applicable to those cases where the source of irritation does not exist in the nerves themselves, but in the organs which they supply, as, for example, in diseases of the lungs, uterus, or stomach. When the cure of these is beyond our skill, we have still to try and mitigate their effects by the administration of sedatives. A certain amount of discrimination is, however, requisite in the selection of the sedative. When the source of irritation is in some part of the nerve centre, which it is not advisable to narcotise, cannabis Indica is, for instance, to be preferred to opium. On the other hand, if it be deemed advisable to produce a sedative effect upon the brain, then opium would be the remedy selected. Again, should the seat of the disease be found to be situated in the pneumo-gastric nerve, conia is preferable to either of the preceding, as it possesses a special narcotic influence on that nerve.

In another set of cases, again, when the digestive organs appear to be at fault, hydrocyanic acid or other remedies of that class may be employed. In fact, as before said, we must suit the remedy to the special case, and when we fail in finding benefit from any particular remedy, we must try the effects of a combination. For it will be constantly found that a mixture of drugs do good, although each had individually failed to make any favourable impression on the disease.

As the majority of cases of diabetes are very chronic, we can easily afford to test the value of the treatment by testing the amount of sugar passed under each remedy, and change from one to the other until a decidedly beneficial result is obtained.

In cases of diabetes from *defective assimilation* we find the same diversity of treatment required. Some improve under the administration of nerve tonics, such as strychnine and phosphoric acid, others are benefited by various preparations of iron, such as the sulphate, iodide, and citrate. Then again we find cases absolutely demanding the free use of both stimulants and sedatives.

In fact, it is exceedingly interesting and instructive to glance over the various plans of treating diabetes which have proved successful in different hands. Thus we find that in one case M. Burquet found that from the first day of the administration of the protoiodide of iron the thirst diminished, the sugar disappeared, and the strength returned.(a)

Denican again declares that he has successfully treated diabetes by giving the patient equal parts of alum and extract of rhatany.(b)

While Semniola speaks with equal confidence regarding the benefits of electricity in the Protean affection.(c)

From all this we draw the important lesson that the disease is in no case to be treated by name, but according to its special requirements.

In concluding these remarks, I must again insist upon the necessity of attending to the three following aphorisms :—

1. In treating cases arising from defective assimilation by restricted diet, although the amount of sugar eliminated may be reduced, we but hasten the termination it is our desire to avoid.

2. In no case ought we to trust to the specific gravity of the

(a) *American Med. Jour.*, January, 1857.

(b) *Gaz. Med. de Paris*, No. 31, 1861.

(c) *Med. Times and Gaz.*, November 9, 1861.

urine alone as an index to the amount of sugar passed, for it is an untruthful guide.

Lastly, we must always bear in mind that in cases of diabetes of the second class (*defective assimilation*) a decided and permanent improvement in the health of the patient is not inconsistent with a temporary rise in the elimination of sugar.

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